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Therapies for Inherited Epidermolysis Bullosa in Indonesia, 2015–2025: A Systematic Review

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Abstract

Background: Inherited epidermolysis bullosa (EB) is a genetic disorder that involves skin fragility caused by structural damage of the sin. In Indonesia, the multidisciplinary care and advanced wound therapies are still limited. A systematic evaluation of published Indonesian EB management strategies is needed to understand current practices and identify gaps in care.

Methods: This is a systematic review gathers case reports, case series, and observational studies from both Indonesian and international databases regarding inherited EB published from 2015 to 2025. Data were taken from each study based on variables such as study design, demographics, EB subtype, clinical features, treatments, and outcomes. Some findings such as clinical features, therapy given and outcomes are extracted narratively because of heterogenicity of the data. Study selection followed PRISMA guidelines.

Results: Thirteen studies were found and reported cases of EBS, DEB, JEB and unclassified EB with clinical findings of extensive blistering, chronic wounds, malnutrition, anemia, infections, and mucosal involvement. Most treatments of wound care (saline compress, petroleum jelly application, cold compresses, and non-adhesive or tulle dressings) resulted in improvements in pain, wound drying, and infection prevention. However, no studies reported the use of advanced wound products, genetic testing, or structured multidisciplinary care. Limited resource constraints and lack of standardized outcome measures were consistent challenges across all reports.

Conclusion: EB management in Indonesia mostly relies on supportive wound care, which is symptomatic treatment, but is still limited compared to international standards that usually prefer advanced dressings, genetic testing, and multidisciplinary care. Improving access to specialized wound-care materials, and developing national EB management pathways are important to bring better results. Future research should focus on cost-effective interventions, long-term monitoring, and standardized evaluation methods.

Keywords: Epidermolysis Bullosa; Indonesia; Therapy; Systematic Review

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1. Introduction

Epidermolysis bullosa (EB) is a genetic disorder that affects the dermo-epidermal junction which makes skin easier to form blisters, with clinical subtypes that vary in severity and systemic complications. Even tough EB itself is rare in the world, cases are recognized across Indonesia, and reporting is increasing through tertiary centers. Clinical management in Indonesia remains largely supportive, such as wound care, infection prevention, nutritional support and prevention of complications. Since curative therapy is not available yet in Indonesia[1–3].

Globally, the therapeutic landscape for inherited EB has evolved since 2015: in addition to optimized wound and symptomatic care, research efforts have advanced gene therapy, protein replacement, cell-based approaches (including stem cell therapies and stromal cell secretome), and clinical trials targeting specific molecular subtypes. However, most emerging therapies remain investigational and are concentrated in high-resource settings; their accessibility, implementation feasibility, safety profile, and evidence base within Indonesia are not well described (5,6).

The present review aims to compile and analyze published case reports and case series of inherited epidermolysis bullosa in Indonesia from 2015–2025, covering all four EB types and focusing on clinical features as well as the treatments given and the results.

2. Material and methods

2.1. Study Design

This review systematically compiles and analyzes published case reports and case series describing inherited epidermolysis bullosa treatment in Indonesia within the past ten years. The methodology used in this systematic review is Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart to maintain quality transparency, as well as reproducibility throughout the reviewing process.

2.2. Search Strategy

This identification phase was conducted using PubMed, Google Scholar, and GARUDA (Garba Rujukan Digital). The search was set to only include studies published between 2015 and 2025. Keywords that are used and applied various Boolean combinations are: "Epidermolysis bullosa", "Epidermolysis bullosa simplex", "Junctional epidermolysis bullosa", "Kindler Syndrome", "Treatment", "Therapy", "Management", "Wound care", "Indonesia" and "Indonesian". Reference lists of all included articles were also screened to identify additional relevant studies not captured through the initial database search.

2.3. Eligibility Criteria

Studies were included if they were carried out in Indonesia, involved human subjects diagnosed with any form of inherited epidermolysis bullosa, and provided clinical, diagnosis, or therapeutic information. Eligible study designs included case reports, case series, and retrospective observational studies published between 2015 and 2025 in Indonesia. Exclusion criteria consisted of studies that did not provide treatment information.

2.4. Study Selection

Records from 2015–2025 were identified using keywords, screened by title and abstract, and duplicates removed. Full-text articles were assessed for eligibility, and thirteen studies met the inclusion criteria. The selection followed PRISMA guidelines.

2.5. Data Extraction

From each included publication, the following information was collected: study design, study location, number of sample (including their gender and age), types of inherited EB, other diagnosed disease, clinical findings, treatment and outcome. Data extraction was performed manually and subsequently cross-verified to minimize errors.

2.6. Data Synthesis

Extracted data were analyzed descriptively using a narrative synthesis approach. Because of considerable variation in study design, sample size, diagnosis, and reporting completeness, quantitative pooling or meta-analysis was not appropriate. Data were categorized into predefined themes, including geographic distribution, clinical features, EB subtypes, other diagnosed disease, clinical feature, treatment and its outcome. Patterns and differences across studies

were examined to illustrate the broader clinical and treatment profile of inherited epidermolysis bullosa in Indonesia. No statistical aggregation was conducted due to the case-based nature of the available evidence.

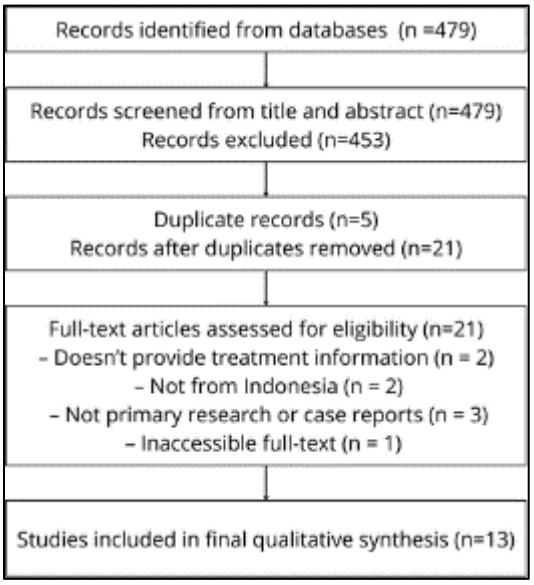

Figure 1 PRISMA Flow Chart

3. Results and discussion

Thirteen eligible studies from various Indonesian regions were included, representing a range of study designs and settings and providing an overview of the current evidence on treatment of inherited epidermolysis bullosa in Indonesia

Table 1 Characteristics of Included Studies

Study	Study Design	Province	Sample and Demographics
Dwiyana et al., 2019 (Study 1)	Single-blind, randomised controlled trial	West Java	4 patients 1-23 years old, All male
Ambarsari et al., 2023	Case Report	Jakarta	1 patient 11 years old male
Widhiati et al., 2022	Case Report	Yogyakarta	1 patient 19 years old female
Heldyani and Sufiatwati, 2023	Case Report	West Java	1 patient 12 years old female
Hertanti et al., 2023	Case Report	East Java	2 patients (twin) 4 months old males
Purnomo and Arifin, 2024	Case Report	Yogyakarta	1 patient 33 weeks old female
Chairisita et al., 2023	Case Report	Jakarta	1 patient 67 years old female
Adisty and Zulkarnain, 2016	Retrospective Study	East Java	2 patients 19 years old female 2 months old male
Dwiyana et al., 2019 (Study 2)	Single-blind, randomised controlled trial	West Java	5 patients

			11-20 years old, 4 males 1 female
Yuniati et al., 2022	Case Report	Central Java	1 patient 21 years old female
Saputra et al., 2022	Case Report	Central Java	1 patient 3 days old female
Amalia et al., 2023	Case Report	Central Java	2 patients 2 days old male 8 days old female
Laksmi et al., 2022	Case Report	Bali	1 patient 8 years old male

Table 2 Clinical Profiles of Patients with Inherited Epidermolysis Bullosa

Study	**EB type**	**Other diagnosis**	**Clinical Findings**
Dwiyana et al., 2019 (Study 1)	EBS (1) DEB (3)	-	-
Ambarsari et al., 2023	EBS	Nephropathy	- Persistent haematuria - Worsening proteinuria - Generalized blisters - Lost his nails - Mitten deformities on hands and feet
Widhiati et al., 2022	JEB	-	- Chronic wounds on philtrum, perinasal and auricular - Decreasing in size but never disappear
Heldayani and Sufiatwati, 2023	DEB	-	- Generalized fluid and blood-filled blisters - Oral: White shallow ulcers, blood vessel rupture, and erythematous lesions
Hertanti et al., 2023	Unspecified (2)	-	Both patients: - Blisters full of fluid since birth from lower extremities that turn into scab.
Purnomo and Arifin, 2024	Unspecified	Pyloric Atresia	- Generalized blisters - Feeding intolerance
Chairisita et al., 2023	DEB	Dyslipidaemia, TB, Chronic venous insufficiency	Recurrent blisters at lower limbs especially after in contact with friction, many damaged nails, recurrent mouth ulcers
Adisty and Zulkarnain, 2016	Unspecified (2)	-	First patient: - Loose, clear blisters that easily rupture and leave erosions in hands, abdomen, back and leg Second patient: - Blisters formed initially at gluteal region, followed by head, trunk, ears and elbow
Dwiyana et al., 2019 (Study 2)	EBS (1) DEB (4)	-	-

Yuniati et al., 2022	Unspecified	Rickets	- Recurrent blisters, - Generalized hypo-/hyperpigmented macules, erosions, crusts, excoriations - Onycholysis - Hair: Partial alopecia, hair squama, stomatitis - Musculoskeletal: Limb bowing, fractures, osteoporosis, scoliosis, knee arthritis, weak muscle - Reproductive: minimal breast development, absent axillary/pubic hair, oligomenorrhea
Saputra et al., 2022	Unspecified	-	Bullous lesions and epidermal damage on feet, gluteal and genital regions
Amalia et al., 2023	EBS (2)	First patient: Amniotic Band Syndrome Second patient: -	First patient: - Generalized blisters after birth, produce yellow clear fluid after ruptured - Skin culture showed *Enterobacter cloacae* Second patient: - Blisters formed on all extremities and abdomen. - Skin culture showed *Staphylococcus aureus* but no signs of infections
Laksmi et al., 2022	DEB	Marasmus type malnutrition	- Generalized lesions originated from blisters filled with fluid from the limbs - It also affects the oral mucosal

Table 3 Therapeutic Interventions and Reported Outcomes

Study	**Intervention/Treatment**	**Outcome/Improvement**	**Outcome category**
Dwiyana et al., 2019 (Study 1)	- Biocellulose wound dressing - Carboxymethyl cellulose wound dressing - NaCl compress	Biocellulose wound dressing and carboxymethyl cellulose wound dressing performed better than normal saline	Partial improvement
Ambarsari et al., 2023	Kidney: - Prednisone -Intravenous Cyclophosphamide - Lisinopril	No longer has proteinuria but still has microscopic haematuria. Kidney functions remained normal until the last check up	Partial improvement
Widhiati et al., 2022	Autologous Non-Cultured Cell Spray with silver-sulfadiazine on plastic wrap	Graft area developed epithelization within 3 weeks then give result of 70% improvement to heal chronic wound	Partial improvement
Heldayani and Sufiatwati, 2023	Skin: -Hydroxyzine - Hydrocolloid - Hydrogel - NaCl compress -Vaseline album Oral: - Topical corticosteroid	Reduced complain of oral pain and blood vessels rupture at a week. Healed erosions, erythema and ruptured blood vessels by 5 weeks. Quality of Life was assessed and shows improvement	Partial improvement

	- Chlorhexidine digluconate mouthwash - Supplements (Vit B12, Folic acid) - Education regarding oral hygiene		
Hertanti et al., 2023	Both patient: - NaCl compress - Topical antibiotic (Fusidic acid and Gentamicin)	First patient: Follow-up examination shows improvement with the blisters of the first baby has dried up Second patient: Forms new blisters	First patient: Partial improvement Second patient: Worsening
Purnomo and Arifin, 2024	Skin: - Topical antibiotic - Antiseptic dressing - Systemic antibiotic Digestive: - TPN - Heineke-Mikulicz pyloroplasty	Patient didn't survive at the 24th day after birth	Death
Chairisita et al., 2023	Skin: - NaCl compress - Topical antibiotic (Fusidic Acid) - Education regarding friction Other: - Simvastatin - Anti-TB - Flavonoid	Patient did regular check up every 2 weeks. Improvement can be seen and no new lesions formed	Partial improvement
Adisty and Zulkarnain, 2016	First patient: - NaCl compress - Antihistamines Second patient: - NaCl compress - Topical antibiotic	-	-
Dwiyana et al., 2019 (Study 2)	- Dialkylcarbamoylchloride-coated Cotton Acetate dressing - NaCl compress + 2% Mupirocin ointment	DACC-coated cotton acetate has better wound closure than normal saline and 2% mupirocin but has same efficiency in eliminating bacterial skin infection	
Yuniati et al., 2022	- Vitamin D - Ceramide moisturizing cream	After vitamin D, fewer skin blisters and no new lesions formed	Partial improvement
Saputra et al., 2022	- Intravenous antibiotics (Ampicillin and gentamicin) - Paracetamol drop - Sterile moist gauze - Topical fucilex cream - Surgical debridement	In 3 days, patient is generally stable, and wounds are clean therefore is discharged.	Partial improvement
Amalia et al., 2023	First patient:	First patient: Discharged at 16 days since he shows improvement from no new blister formation and dried out lesion	Both patients: Partial improvement

	- Topical antibiotic (Fusidic acid and Silver sulfadizine) - Ampicillin Second patient: - Topical antiboitic (Fusidic acid and Silver sulfadizine) - Erythromycin - NaCl compress	Second patient: Discharged after 10 days due to clinical improvement	
Laksmi et al., 2022	Skin: - NaCl compress - Petroleum jelly - Tulle -Gauze Malnutrition: - Amoxicillin - Neocate junior - Vitamin A	After 30 days, many lesions dried up and no new lesion formation and no fever.	Partial improvement

3.1. Epidemiological and Study Characteristics

There are thirteen studies found that fulfills the eligibility criteria (7–19). Every study except for 1 was originated from the Java Island, while the other 1 was from Bali. This suggests that EB cases seen in tertiary care centers are more likely to be documented, whereas cases from rural or remote regions may remain underreported, since most tertiary care are dominantly from the Java Island (20). The national clinical practice guidance from PERDOSKI also stated that one of the interventions is to referred to a higher tier of health services (4).

Almost all studies found were case reports, with 2 randomized controlled trial and 1 retrospective study. reflects the rarity of EB and the limited diagnostic and reporting cases in the country as well as a methodological gap in Indonesian EB research about EB itself.

3.2. Clinical and Diagnostic Patterns

The clinical profiles extracted from the included studies reveal a mixture of Epidermolysis Bullosa Simplex (EBS), Dystrophic Epidermolysis Bullosa (DEB), and Junctional Epidermolysis Bullosa (JEB). Many of them are also still unspecified, probably due to the lack of a more advancing diagnostic tools such as genetic testing or immunofluorescence antigen mapping. A previous study in Bandung shows only 33% of patients were correctly diagnosed after genetic assessment (21). This shows how clinical diagnosis alone still can misclassify EB subtypes, which then leads to limiting optimal prognostication and individualized care.

The need of precise diagnosis is clear in the case report of recessive dystrophic EB–mitis in an elderly patient, where immunofluorescence was found negative for immunoglobulins that helps cross out the differential diagnosis which are autoimmune blistering diseases (13). This confirms that even within DEB variants, there can be atypical presentations that are easily misdiagnosed without proper tools.

Complications observed in Indonesian patients are like the one those reported in international EB cohorts, such as generalized blistering, chronic erosions, infection, nutritional deficiency, and pseudosyndactily (webbing of fingers/toes). For example, the pediatric case of severe RDEB with marasmus-type malnutrition was reported, shows severe untreated EB can also affect multisystem [19].

Parenting factors also play a significant role, a recent Indonesian study assessed parental awareness of oral health in children with EB; while baseline knowledge was acceptable, the study highlighted the difference in perception of oral-health-related quality of life and the need for education and preventive dental care (22). These results reflect to the known mucosal and dental complications in EB and the need for multidisciplinary care.

3.3. Therapeutic Approaches in Indonesia

The treatments reported in Indonesian studies mostly are symptomatic, focused on wound care, and still aligned with global standards, even though curative therapies are still absent. A key point of EB wound management is creating an trauma free environment, such as maintaining a moist but non-infected wound bed as well as minimizing friction.

Although there is limited published data on advanced dressings used in Indonesia, reports and wound-care practice descriptions suggest that mostly treated by saline compress (0.9% NaCl), petroleum jelly, non-adhesive gauze (e.g., tulle), and frequent dressing changes. These are low to moderate cost interventions to adapt to the local economy. One of the case reports noted that NaCl compresses every 8 hours, combined with petroleum jelly and simple gauze coverage, successfully shows clinical improvement in wound appearance and reduced blistering [19].

When we compare this with more worldwide evidence, a recent systematic review and meta-analysis of topical treatments in EB demonstrated that dressings such as Oleogel S-10 (birch bark extract), biocellulose, and other silicone-based or polymeric dressings show faster wound healing time and improved outcome [3]. This suggests that Indonesia could benefit from wider choice to adopt from more advanced topical agents, though cost and availability should still be considered.

National organization like DEBRA Indonesia, plays an important role in advocacy, patient support, and the distribution of care guidance. Their involvement is essential in low-resource environment because they make sure help is still accessible there.

3.4. Outcomes, Limitations and Challenges

The outcomes of the therapy reported in Indonesian case studies are notable but still limited: mostly reported partial improvement such as progressive wound healing, reduced blister frequency, or improved skin condition, which are still considered short-term based on the follow up time. Long-term outcomes such as impact on quality of life, functional status, or survival are still rarely reported.

This could happen because of several factors such as:

- **Under-performance reporting:** The rarity of EB mean many patients will never receive a definitive diagnosis or be reported in the literature. This is shown by the data suggest that at 2021, only 66 EB patients were documented in Indonesia with the help of DEBRA Indonesia [23].
- **Resource constraints**: Although simple dressings and saline are commonly used, but still compared to topical therapies, they have a disadvantage in wound healing. This is due to how topical therapies are still more expensive that makes them less accessible.
- **Multidisciplinary care gaps**: While wound care is foundational, EB management also requires multidisciplinary team that include nutritionists, dentists, physiotherapists, and psychosocial support. One of the studies illustrates that some of these dimensions (dental care) are already under-addressed [22].

3.5. Integrated Interpretation

This systematic review synthesizes therapeutic approaches for inherited epidermolysis bullosa (EB) in Indonesia from 2015 to 2025. Despite the rarity of EB, the Indonesian literature demonstrates a diverse clinical spectrum, including epidermolysis bullosa simplex (EBS), dystrophic epidermolysis bullosa (DEB), junctional epidermolysis bullosa (JEB) and several unclassified EB cases [7–19]. This may be caused by the fact that advanced diagnostic techniques in Indonesia like immunofluorescence antigen mapping and genetic testing are still rare. This limitation echoes findings from a genotype–phenotype correlation study in Indonesia, which prove the point of importance of gene testing, that found multiple mismatches between clinical and genetic diagnoses [13]. In the rest of the world, accurate EB classification mostly relies on genetic testing due to for a more specific care and therapy [24,25].

Therapeutic interventions reported in Indonesia are still mostly wound care which are still consistent with international management guidelines[26]. The most used modalities include saline cleansing, petroleum jelly, cold compresses, and non-adhesive dressings. Even though they are simple, these interventions were proven to have beneficial outcomes, such as reduced blistering, improved wound drying, decreased pain, and fewer infections based on the several studies [7–11,13,15–19]. This shows the fundamental principle of EB care: reducing mechanical friction, maintaining moist wound environments, and preventing secondary infection are successfully implemented in Indonesia.

However, compared with global EB practice, Indonesian care is still behind in terms of the lack of advanced wound care treatments. International literature supports the use of tissue-engineered skin, collagen, fibroblast accelerated wound healing [3]. More recent innovations such as birch bark extract (Oleogel-S10) have shown promise for partial-thickness wounds in EB [3], yet none of these modalities appear in Indonesian studies, most likely due to cost, availability, and lack of insurance coverage. This difference shows that a better economy can access better treatments, while middle-income can't.

Most of the outcomes from the treatment reported from the studies are positive, but they are limited by the absence of standardized assessment tools for wound severity, pain, and quality of life. The reports also have short follow-up durations, and lack long term evaluation of the wound healing, scar formation, or functional impairment. Despite these limitations, the consistent improvements observed with structured wound care proves the importance of sustained, multidisciplinary management.

Wider systemic challenges in Indonesia include limited access to genetic testing, a lack of health care to treat EB, unavailability of specific dressings, and insufficient integration of nutritional, dental, as well as psychosocial care. Studies assessing parental awareness of oral health for EB patients in Indonesia further shows the lack in caregiver education and dental support[10]. In comparison, global guidelines emphasize routine dental evaluation, nutritional assessment, and early physiotherapy to prevent long-term morbidity [4,26].

Given these findings, several priorities emerge for future development. Establishing a national EB registry would help in accurate epidemiological mapping as well as resource planning. Expanding access to immunofluorescence mapping and genetic testing would lead to accurate diagnosis that would then lead to specific care and treatment. Local research to comparing cost-effective dressing options including evaluating affordable alternatives to silicone or advanced dressings is essential for a resource limited environment, or to find another effective treatment from Indonesia's rich natural resources. Finally, improving multidisciplinary EB care pathways and expanding public health insurance coverage for supplies would improve patient outcomes.

In summary, EB management in Indonesia aligns with global principles but still limited from the many aspects such resource and long-term multidisciplinary care. Addressing these needs through national policy, clinical infrastructure strengthening, and locally relevant research is important to improve outcomes for Indonesian EB patients.

4. Conclusion

This systematic review highlights that the management of inherited epidermolysis bullosa in Indonesia still are mostly supportive, with wound care focused on simple, accessible treatments such as saline cleansing, petroleum jelly, and non-adhesive dressings. Although these approaches consistently demonstrated improvements in blister control, wound drying, infection reduction, and patient comfort, there are still the absence of advanced wound-care treatments and multidisciplinary care limits the overall quality of care. Indonesian EB cases also frequently showed with complications such as malnutrition, anemia, recurrent infection, and functional impairment reflecting both the severity of the disease and lack in long-term comprehensive management.

To improve outcomes, national efforts are needed to improve accessibility specialized dressings, as well as strong multidisciplinary EB care pathways, and develop a structured system for epidemiological and clinical monitoring. Future research should prioritize locally relevant, cost-effective interventions and standardized outcome measures or alternative resources. By addressing these systemic and resource-related challenges, Indonesia can move toward more evenly distributed and evidence-based care for patients living with epidermolysis bullosa.

Compliance with ethical standards

Disclosure of Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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