Recessive Dystrophic Epidermolysis Bullosa and Disease Burden: Changes in Patient Life Quality

Marcela Yasmin Veiga Biset Oliveira [a]

[a] Bahiana – School of Medicine and Public Health (EBMSP), Salvador, Bahia, Brazil, marcelaoliveira22.2@bahiana.edu.br

Abstract. Recessive dystrophic epidermolysis bullosa (RDEB) is a skin disorder characterized by fragility and blistering, along with extracutaneous manifestations that significantly impact the quality of life (QoL). These effects are not limited to the clinical aspects but also include economic and social consequences. To describe how the disease affects individuals throughout different stages of life and highlight age-specific concerns, a literature review was conducted using medical databases such as PUBMED and Science Direct. The review revealed that, although the disease imposes burdens similarly across age groups, teenagers and young adults report greater economic impacts, particularly related to the costs of treatment, such as clothing and hospitalizations. In contrast, children face social challenges, including bullying and overprotective parenting, which can hinder academic performance and mental health. This academic difficulty is often mistakenly attributed to cognitive impairment rather than social factors. Life expectancy in individuals with RDEB is reduced, primarily due to a high risk of developing squamous cell carcinoma (SCC) and other severe complications, including issues related to immune function, dental health, cardiovascular, musculoskeletal, and metabolic systems. Further studies are needed to investigate the impact on the QoL of older adults and the elderly with RDEB, as well as to examine how factors such as socioeconomic status and gender influence the disease's effects across different populations, as well as different impacts associated with economic burden, such as targeting ways to compare low-income and high-income countries.

Keywords. Recessive Dystrophic Epidermolysis Bullosa; Disease Burden; Quality of Life

1. Introduction

Dystrophic epidermolysis bullosa (DEB) is one form of an extensive group of conditions called epidermolysis bullosa, which causes the skin to be fragile and blister easily, even from minor injury or friction. The recessive dystrophic epidermolysis bullosa (RDEB) form is a severe type of DEB, characterized by mutations in alleles of *COL7A1*, a gene responsible for producing type VII collagen (C7) (1). These mutations cause alterations in the structure and number of anchoring fibrils, which are responsible for securing the dermal layer of the skin to the epidermal layer (2). RDEB is considered more severe, as blistering and erosions affect the entire body, while the dominant form (DDEB) is usually limited to the hands, feet, knees, and elbows, where blistering is often mild (3).

This condition affects the quality of life (QoL) in physical, emotional, and social aspects, and, compared to other dermatologic diseases, QoL is significantly impacted in individuals with RDEB, especially regarding economic burdens on younger patients (4). Although most studies discuss the current impact on adult patients, they do not address how economic burdens and QoL change over the years, nor how the condition affects children differently, including aspects such as friendships and bullying, which are important factors for their well-being. Therefore, the aim of this study is to address these topics, discussing the various forms of burden that RDEB may present, particularly how these burdens evolve throughout a person's lifetime.

2. Methodology

The present study is a literature review primarily utilizing the PUBMED database, but it also includes articles from Science Direct. A total of 22 articles sparked interest, and, in the end, 13 were selected. The excluded articles were omitted because they did not directly address the theme or discussed other topics, such as immunopathology or pharmacological treatments, that do not align with the aim of this study. The search was conducted using the Boolean operator AND, with the search terms "dystrophic epidermolysis bullosa, autosomal recessive," "recessive dystrophic epidermolysis bullosa," "RDEB," "disease burden," "disease cost," "cost of illness," "life expectancy," "quality of life," "life quality," and "bullying."

3. Results

RDEB impacts various aspects of an individual's life, creating both a clinical burden and a subjective burden, both of which affect quality of life. Firstly, the burden of pain and itch, with high levels of pain and pruritus compared to patients with DDEB and other skin diseases, also characterizes the wound burden, as the fragility of the skin tends to maintain chronic wounds that remain open for 12 weeks or more (1). Additionally, as shown in Table 1 below, other extracutaneous manifestations also occur, such as the risk of severe injury to the bone marrow, musculoskeletal system, heart, kidneys, and teeth (5). It is important to note that the lifetime risk of aggressive squamous cell carcinoma (SCC) is greater than 90%, with significant metastatic potential. Other manifestations may also impact children's development, such as psychological alterations related to their perception of their own body and mobility (5). As a result, the clinical burden begins to interfere with the subjective burden, where impacts on daily activities or comments made by peers can cause anxiety and depression.

Tab. 1 – Extracutaneous manifestations of DEB.

Musculoskeletal	Dental	Other
Fusion of the digits	Blisters and erosions	Anemia
Mitten deformities	Prolonged clearance of food	Prone to infections due to innate barrier lesion
Reduced fine manipulative skill and digital prehension	Intraoral soft tissue scarring	Delayed puberty
Generalized osteoporosis	Premature loss of dentition	Susceptibility to cancer

Regarding RDEB, children reported being completely dependent on major activities of daily living (ADL), with 26% of them dependent on bathing, 20% on grooming, 13% on dressing and walking, and 2% on toileting and feeding (6). Another study conducted on teenagers and young adults (around 17-21 years old) showed that the burden of dressing affects the economic situation of 50% of the interviewees, due to the cost of dressing materials and the time spent on changing, as well as medical expenses (7).

Moreover, participants in another study with severe EB reported a loss of spontaneity due to time-consuming care, preventing them from participating in activities such as socializing. Bullying was reported as one of the most frequent school interactions, with avoidance and teasing being common, as well as coping with intrusive questions and overprotective caregivers. This contributes to gaps in academic knowledge, which are often misattributed to cognitive impairment (8). Additionally, when these emotional aspects were discussed in older age groups, depression and suicidal ideation appeared to increase with age due to the growing economic burden, which becomes more evident as individuals become independent (5). Finally, life expectancy is reduced due to the development of SCC, which has a high propensity for metastasis and typically develops in chronic wounds and scarring sites, posing a significant threat to individuals suffering from large chronic wounds (9).

4. Discussion

The disease burden impacts all age groups in a somewhat similar manner, associated with the manifestations of the cutaneous form of the disease, which may impact daily activities such as walking, eating, and getting dressed. Some particularities are important in children, such as the impact of bullying on their mental health and educational development, given the frequent hospitalizations and negative impacts of mean comments. How teachers handle situations regarding their students is also a key factor in the children's interest in class; therefore, they should convey information and knowledge regarding the importance of understanding this condition, rather than trying to separate children from contact with RDEB-affected peers. That is why, for an inclusive educational environment, it is important to understand that these individuals need to be integrated into society and not pushed away by it, aiming to reduce educational gaps between students and to decrease the hostile atmosphere towards these peers. Overprotective caregivers also represent a burden for these children, which should be addressed during health services, as it may inhibit the child from experiencing things other children do, as well as create an environment for the development of associated anxiety disorders and impacts on social functioning in adolescence (10).

Meanwhile, QoL assessment on teenagers and young adults showed that, on top of the clinical and subjective burden expressed previously, the economic burden starts to manifest more, especially regarding access to medical care, treatment, and materials that need to be used by these individuals, such as clothing materials. It is questioned how unfavourable economic conditions in low-income countries affect the life expectancy of these individuals, as access to healthcare is more challenging. This is highlighted as a limitation expressed in various articles, given that malnutrition is also presented as a significant comorbidity associated with RDEB (11), as well as gastrointestinal consequences, which can impact growth (3). This is extremely relevant, since social inequities are expressed even in disease, where middle-income to high-income countries have better access to health care and favourable social conditions, such as access to information.

Disease burden in something that is expressed differently and is measured by disability-adjusted life years (DALYs), where the rates were 44% higher in poor-income countries, especially in nutritional conditions (12), but it's correlation to RDEB was not further investigated. It is an important matter that needs more research since the addition of the years lived with disability with years of life lost expresses what could be changed during the disease's management, sometimes extremely precarious when the needs of low-income countries are ignored. It also is useful to address QoF, something that is severely affected by RDEB.

Regarding mental health, although it is well characterized, the different impacts related to sex usually have small sample sizes, producing inconclusive results (4,13). It is important that this issue is addressed, as different gender norms affect sexes differently, with other inherited and autoimmune blistering diseases contributing to higher psychological morbidity in female patients, especially due to social pressures on women's appearance (13). Furthermore, the population aged 25 years and older has not been addressed in population studies assessing quality of life, making it difficult to determine how the burden progresses in this age range. However, it is implied that the increased risk of associated morbidities and SCC negatively impacts their life expectancy.

5. Conclusion

These results imply that although the disease burden is present in younger and older individuals, it is manifested a bit differently across different age groups. These different highlights urge for age-specific strategies that aim to It also implies that ignorance about skin conditions and the lack of preparation of professionals in the areas of education and health contribute to less integrated individuals during their development as children, which can impact them negatively. However, the limitations regarding social determinants of health, such as economic conditions, job conditions, and housing conditions were not addressed, as well as different aspects such as gender, older societal groups and impacts on different regions of the world need further investigation.

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