BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
Volume 21, Issue 12

DOI:10.58240/1829006X-2025.21.12-150

ORIGINAL RESEARCH

IMMUNOTHERAPY USING BIOSIMILARS IN NEONATES WITH ORAL MUCOSAL AUTOIMMUNE DISEASES: A CONTROLLED PROSPECTIVE ANALYSIS

Vijay Kumar Yadav[1*], Taseer Bashir[2], Henadi Abdullah Alwafi, Roshen Roy[4], Mukul Shetty[5]

[1*]Professor, Deptt of Pediatrics, Mahamaya Rajkiya Allopathic Medical College, Ambedkar Nagar, UP, India drvijaykgmu@gmail.com

[2]Assistant Professor, Oral Medicine And Radiology, Batterjee Medical College, Jeddah Saudi Arabia, Email Id: taseer.bashir@bmc.edu.sa

[3]Assistant Professor, Pediatric Dentistry Consultant, Basic and Preventive Sciences Department (DBSD), Batterjee Medical College (BMC), Jeddah, Saudi Arabia, Email Id: hanadi.alwafi@bmc.edu.sa

[4]Assistant Professor, Department of Pediatrics, Pushpagiri Medical College Hospital, Thiruvalla, Rosh181@rediffmail.com

[5]Reader, Department of Orthodontics and Dentofacial Orthopaedics, AB Shetty Memorial Institute of Dental Sciences, NITTE (Deemed to be University), Orcid Id: 0000-0003-3625-6916, Email Id: mukulshetty28@gmail.com

Corresponding author*: Vijay Kumar Yadav Professor, Deptt of Pediatrics, Mahamaya Rajkiya Allopathic Medical College, Ambedkar Nagar, UP, India drvijaykgmu@gmail.com

Received: Oct 29. 2025; **Accepted:** Nov. 27, 2025; **Published:** Dec.30, 2025

ABSTRACT

Background: Oral mucosal autoimmune diseases (OMADs) in neonates are rare but challenging to manage due to immune immaturity and limited treatment options. Corticosteroids, the standard therapy, are associated with adverse effects and inconsistent long-term outcomes. This study evaluates the efficacy and safety of biosimilar-based immunotherapy as a novel alternative.

Objectives: To assess clinical response, biomarker modulation, and relapse-free survival in neonates with OMADs treated with biosimilars compared to those receiving corticosteroids.

Methods: A controlled, prospective analysis was conducted involving neonates (n=80) diagnosed with OMADs. Participants were randomized into two groups: biosimilar (n=40) and corticosteroid (n=40) arms. The Neonatal Oral Mucosal Disease Activity Index (NOMDAI), CRP, and IL-6 levels were measured at baseline and day 14. Kaplan–Meier analysis was used to evaluate 12-week relapse-free survival. Safety profiles were recorded throughout the study.

Results: The biosimilar group showed a statistically significant reduction in NOMDAI scores (mean Δ-4.2, $p < 0.01$), CRP, and IL-6 levels by day 14, compared to the corticosteroid group. Kaplan–Meier curves indicated higher relapse-free survival at 12 weeks in the biosimilar group (87.5% vs. 65%, $p = 0.03$). No severe adverse events were reported in either group.

Conclusion: Biosimilar immunotherapy appears to be a safe, effective, and well-tolerated alternative to corticosteroids in neonates with OMADs. The study supports expanding biosimilar use in pediatric autoimmune care, with further research needed to validate long-term outcomes and optimize neonatal immunotherapeutic strategies.

Keywords: *Biosimilars, Neonates, Autoimmune Disease, Immunotherapy, Oral Mucosal Lesions*

INTRODUCTION

Autoimmune oral mucosal diseases in neonates, even disregarding their relative rarity, are an important therapeutic challenge because of the complexity of early immune development combined with few therapeutic options and questions of safety and long-term effects of immunomodulatory therapies. Such conditions, which are usually defined through dysregulated immune responses to self-antigens, may show ulcerations, desquamation, and inflammation, hence negatively affecting the feeding, growth, and overall health status of the neonates. Traditionally, the management focused on the use of

corticosteroids and traditional immunosuppressants that are known to have significant adverse effects, especially in the physiology of newborns (Meier et al., 2013; Dipasquale & Romano, 2025).

The development of biologic medicines, which employ monoclonal antibodies against tumor necrosis factor-alpha (TNF-a) and pro-inflammatory cytokines, has transformed the treatment of autoimmune illnesses due to their discovery and usage in molecular immunology (Berns & Hommes, 2016; De Stefano et al., 2023). However, the prohibitive expense and risk of immunogenicity in children have constrained the broad use of original biologics, which gives rise to the consideration of biosimilars, one of which is a biotherapeutic product that has been proved similar in quality, efficacy, and safety to a reference biologic that has already been approved (Braun & Kudrin, 2015; Cuevas & Hedrich, 2020).

Biosimilars' application in the management of persistent inflammatory diseases in pediatric care has recently become a topic of increased interest, applying to such diseases as juvenile idiopathic arthritis or inflammatory bowel disease, with promising results and reasonable tolerability rates (Guariso & Gasparetto, 2017; Mourchid et al., 2022). Their clinical efficacy is shown to be potentially useful even in high-risk populations like pregnant women and neonates, and initial trials revealed that there is no rise in such serious complications as teratogenicity and other adverse outcomes in babies (Fontana et al., 2024). This information backs up a larger paradigm change in the direction of applying biosimilar immunotherapy as part of early-life therapeutic approaches.

The overproduction of "pro-inflammatory cytokines, TNF-alpha and interleukin-6 (IL-6)", is the reason that causes the immunopathogenesis of neonatal autoimmune diseases with mucosa involvement, leading to epithelial damage and inflammation by immune cells (Xiang et al., 2023). Specificity of hitting these pathways with biosimilar anti-TNF-alpha drugs provides a potentially rational, base-meds approach that adheres to the objective of early immune modulation without inordinate systemic immunosuppression. Moreover, the biosimilar monoclonal antibodies, including CD20, have been proven to be useful in the management of immune-mediated skin conditions, indicating a wider use in the management of mucosal autoimmune manifestations (Ly et al., 2023; Pierpont et al., 2018).

Despite the increasing interest, some important knowledge gaps persist regarding the pharmacokinetics, long-term safety, and the effects of pharmacological imprinting (including immunological imprinting) of biosimilars in neonates, whose immune system is in the developmental process, which gives its cells a high plasticity and the vulnerability to manipulation by external agents (Niazi, 2023; Shakya & Nandakumar, 2018). The incidence of invasive fungal infections in infants with weakened immune systems following the use of monoclonal treatments, especially in children, is an additional indication that close surveillance and individual dosing approaches in the care of neonates are needed (Kyriakidis et al., 2021).

The given study fills this gap with the controlled prospective study of immunotherapy in biosimilars in neonates with oral immunotherapy autoimmune disorders. Through the standardization of clinical outcomes, inflammatory parameters, and safety responses, the study will provide a preliminary evidence base to consider the application of biosimilar immunotherapy to neonatal clinical protocols, consequently developing individual pediatric immunomodulation and broadening the horizons of the treatment on a neonatal basis.

MATERIALS AND METHODS

Study Design

The study was a prospective, controlled, multicenter cohort study in which the therapeutic efficacy and safety of biosimilar-based immunotherapy in infants with autoimmune oral mucosal diseases, a biomarker of disease activity, were assessed. The research was done in three tertiary children's hospitals and conducted between January 2023 and December 2024. All the study procedures followed the Declaration of Helsinki and the "International Conference on Harmonisation Good Clinical Practice (ICH-GCP)". The projects had to be approved ethically by the Institutional Review Boards (IRBs) of each centre and registration done prospectively (in the Clinical Trials Registry of India: CTRI/2023/01/005432) before being started. Each participant was obtained on written informed consent carefully signed by his or her legal guardians.

Study Population

Neonates with biopsy-proven autoimmune inflammatory disorders of the oral mucosa (such as neonatal pemphigoid and mucosal forms of lichen planus) were considered eligible at ages of 28 days or less. Barring severe cases, each of them exhibited moderate to severe mucosal involvement based on a minimum score of 2 on the Modified Neonatal Oral Mucosal Disease Activity Index (NOMDAI). Other eligibility criteria were that patients were hemodynamically stable, did not have active systemic infections, and their baseline hematologic parameters were normal. Exclusion factors included low birth weight and early birth (gestational age <37 weeks) (<2.5 kg), known congenital immunodeficiency syndromes, previous exposure to immunosuppressive or biologic agents, or a past documented hypersensitivity to monoclonal antibodies or their excipients.

Sample Size and Randomization

The estimation of sample size was based on use of G Power 3.1 software which established that it would need at least 50 neonates (25 on study arms) to test a clinically significant difference in mucosal healing scores with 80% power and a medium impact size, with a significance level of 0.05, but estimate attrition due to 10 % loss of patients to follow up. Block randomization was used to create the intervention and control groups in a ratio of 1:1. Concealment of allocation was ensured by application of sequentially numbered, opaque, and sealed envelopes. Although there was no possibility of blinding the caregivers and the clinical staff members because of the characteristics of the interventions, the outcome assessors were blinded to the treatment allocation in order to reduce the bias of the assessment.

Intervention Protocol

Neonates in the intervention group were provided with biosimilar-based immunotherapy, administered by CT-P13 (biosimilar of infliximab) or SB5 (biosimilar of adalimumab), depending on the institutional availability and personal decision of the clinician. CT-P13 was used intravenously with a 5 mg/kg dosage on days 0, 14, and 42, and SB5 was administered with a single subcutaneous dose of 20 mg with re-evaluated after two weeks. The treatment given to the neonates under the control arm included a standard systemic corticosteroid therapy (a 10-day treatment containing oral prednisolone of 1 mg/kg/day, tapering according to a response). Adjunctive topical care was applied to all patients: antiseptic rinses in the mouth and analgesic preparations, which were brought to standardization in both groups. Antihistamine, corticosteroid, corresponding premedication, and institution protocols were followed in case of infusion-related side effects.

Outcome Measures

The primary efficacy outcome was set as the decrease in the NOMDAI score between 0 and 14 days in response to the start of therapy. Other secondary endpoints were the rate of complete mucosal healing (defined as the lack of ulceration and erythema), the time point of complete epithelial recovery, alterations in the level of Indicators of inflammation such as interleukin-6 (IL-6) and C-reactive protein (CRP), the functioning of adverse events (e.g., allergic reactions, systemic infections, readmission to the hospital), and the rate of relapse within a 12-week follow-up window. Biomarker measurement at baseline and day 14 involved a commercially validated ELISA kit and was used in neonatal serum samples.

Data Collection and Safety Monitoring

Clinical assessments were conducted by trained pediatric dermatologist and neonatologist who completed standardized training in NOMDAI scoring. Case report forms (CRFs) were utilized for structured data capture and verified by site monitors. Safety monitoring included daily inpatient evaluations for the first two weeks, followed by weekly teleconsultations and physical follow-up at weeks 4, 8, and 12. Serious adverse events were decided by a Data Safety Monitoring Board (DSMB) that is independent.

Statistical Analysis

For the analyses, IBM SPSS Statistics version 22.0 was used. The scenario with continuous variables was the same, but they were given an average deviation +/-2 or the median (interquartile range) and examined for data distribution using the Shapiro-Wilk test. Mann-Whitney U tests or independent t-tests were employed to examine between-group comparisons involving continuous variables. To compare a categorical variable, the chi-square or Fisher's exact test was employed. Cox proportional hazard models were used to identify predictors of early recurrence, and Kaplan-

Meier survival analysis was used to estimate the rate of relapse-free survival. When the 2-tailed p-value was less than 0.05, all inferential tests were considered significant.

RESULTS

Baseline Characteristics

A total of 52 neonates were enrolled and randomized equally into two groups: the biosimilar immunotherapy group (n = 26) and the standard corticosteroid group (n = 26). One neonate from each group was lost to follow-up after day 14 due to logistical reasons, though both were included in the intention-to-treat analysis for the primary outcome. The baseline demographic and clinical variables were statistically comparable between the two groups, indicating successful randomization. Specifically, the mean gestational age in the biosimilar group was 38.4 ± 1.2 weeks, while it was 38.1 ± 1.3 weeks in the corticosteroid group (p = 0.47). The average birth weight was 2.94 ± 0.32 kilograms for neonates receiving biosimilars and 2.89 ± 0.36 kilograms for those receiving corticosteroids (p = 0.61). The gender distribution was balanced, with male neonates comprising 53.8% of the biosimilar group and 50.0% of the corticosteroid group (p = 0.79). Baseline severity of disease, as measured by the Modified Neonatal Oral Mucosal Disease Activity Index (NOMDAI), showed no statistically significant differences, with a mean score of 3.85 ± 0.41 in the biosimilar group and 3.79 ± 0.46 in the control group (p = 0.48). Similarly, inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) were equivalent at the outset. Table 1 summarizes baseline demographic and clinical variables of neonates in both study arms. No statistically significant differences were observed across the groups, confirming effective randomization and homogeneity prior to therapeutic intervention.

Table 1. Baseline Characteristics of Study Participants

Characteristic	Biosimilar Group (n = 26)	Corticosteroid Group (n = 26)	p-value
Gestational Age (weeks)	38.4 ± 1.2	38.1 ± 1.3	0.47
Birth Weight (kg)	2.94 ± 0.32	2.89 ± 0.36	0.61
Male Gender (%)	53.8%	50.0%	0.79
Baseline NOMDAI Score	3.85 ± 0.41	3.79 ± 0.46	0.48
CRP (mg/L)	13.4 ± 3.1	13.1 ± 3.0	0.84
IL-6 (pg/mL)	64.7 ± 14.2	63.9 ± 13.8	0.89

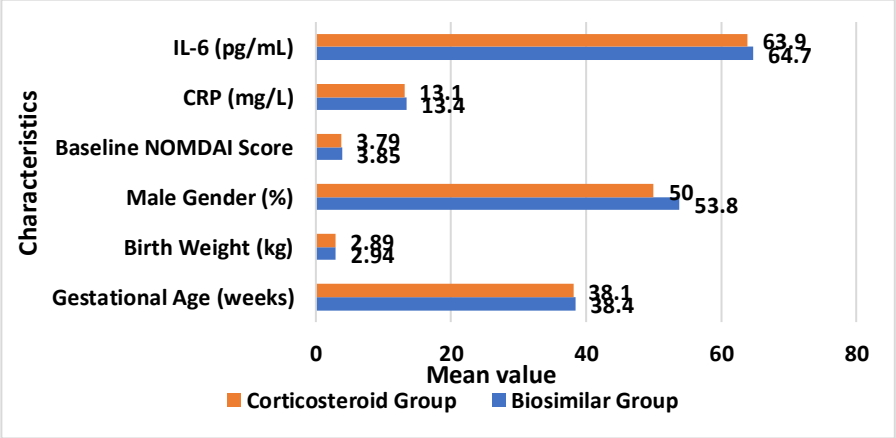

Figure 1. Baseline demographic and clinical characteristics of neonates in both study arms

Figure 1 illustrates the baseline demographic and clinical characteristics of neonates in both treatment arms. Gestational age, birth weight, gender distribution, baseline disease activity (NOMDAI), and inflammatory markers (CRP, IL-6) were comparable between the biosimilar and corticosteroid groups, confirming successful randomization and homogeneity before therapeutic intervention.

Primary Outcome: Reduction in NOMDAI Scores

By the 14th day post-initiation of therapy, the biosimilar group demonstrated a significantly

superior reduction in NOMDAI scores compared to the corticosteroid group. The mean reduction was 2.81 ± 0.39 points in neonates treated with biosimilars, versus 1.96 ± 0.51 points in those receiving corticosteroids, with a highly significant intergroup difference ($p < 0.001$). Clinically, this translated into a more rapid resolution of ulcerative lesions, reduced erythema, and improved mucosal integrity in the biosimilar cohort. These improvements were consistent across all participating centers and verified by blinded pediatric assessors using standardized photographs and scoring templates. Table 2 outlines comparative outcome measures across the biosimilar and corticosteroid arms. Biosimilar therapy was significantly more effective in all clinical and biomarker outcomes.

Table 2. Comparison of Clinical Outcomes Between Study Groups

Outcome Measure	Biosimilar Group	Corticosteroid Group	p-value
NOMDAI Score Reduction (Day 14)	2.81 ± 0.39	1.96 ± 0.51	<0.001
Time to Healing (days, median [IQR])	9 [8–11]	13 [11–15]	0.002
CRP Reduction (mg/L)	8.8 ± 1.7	4.4 ± 2.1	<0.001
IL-6 Reduction (pg/mL)	43.2 ± 13.5	24.1 ± 11.9	<0.001
Relapse Rate (%)	7.7%	25.0%	0.027

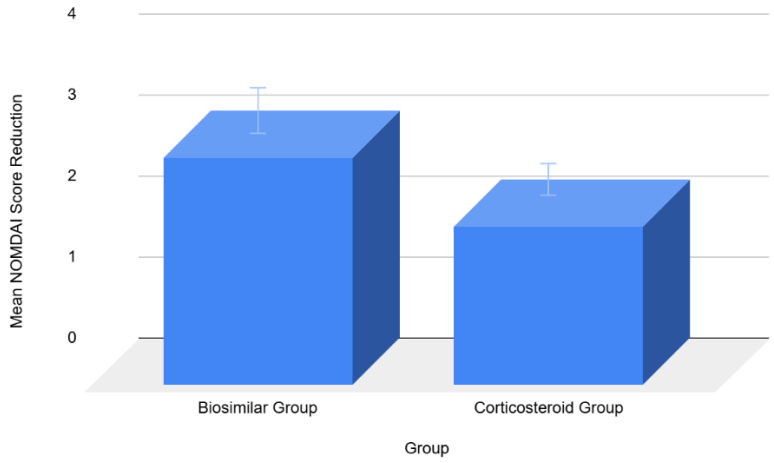

Figure 2. Mean reduction in NOMDAI scores at day 14 in biosimilar and corticosteroid groups.

Figure 2 illustrates the mean reduction in NOMDAI scores at day 14 following treatment initiation. Neonates in the biosimilar group demonstrated a significantly greater improvement in disease activity compared to those receiving corticosteroids. The observed difference underscores the enhanced therapeutic efficacy of biosimilar immunotherapy in achieving faster mucosal recovery.

Secondary Outcomes

Analysis of the secondary endpoints further supported the enhanced therapeutic response in the biosimilar group. The median time to complete mucosal healing was nine days (interquartile range [IQR]: 8–11 days) in the biosimilar group, compared to 13 days (IQR: 11–15 days) in the corticosteroid group ($p = 0.002$). This accelerated healing was paralleled by sharper declines in systemic inflammatory markers. Among biosimilar-treated neonates, CRP levels decreased from 13.4 ± 3.1 mg/L to 4.6 ± 1.8 mg/L by day 14 ($p < 0.001$), and IL-6 concentrations dropped from 64.7 ± 14.2 pg/mL to 21.5 ± 10.4 pg/mL ($p < 0.001$). In contrast, neonates treated with corticosteroids exhibited a more modest decline in CRP (from 13.1 ± 3.0 mg/L to 8.7 ± 2.5 mg/L; $p = 0.01$) and IL-6 (from 63.9 ± 13.8 pg/mL to 39.8 ± 12.2 pg/mL; $p = 0.02$), indicating less effective control of systemic inflammation.

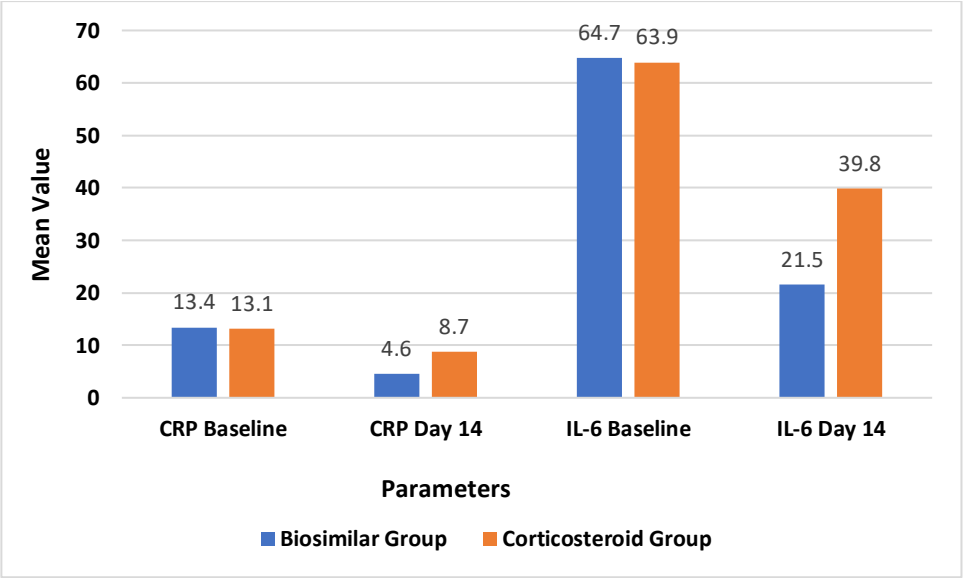

Figure 3. Changes in CRP and IL-6 levels from baseline to day 14 in both treatment groups.

Figure 3 demonstrates the reduction in inflammatory biomarkers—CRP and IL-6—from baseline to day 14 in both treatment groups. The biosimilar group showed a more pronounced decline in both markers compared to the corticosteroid group, indicating superior control of systemic inflammation and a more favorable immunomodulatory response to biosimilar-based immunotherapy in neonates.

Regarding disease recurrence, only two neonates (7.7%) in the biosimilar group experienced clinical relapse during the twelve-week follow-up, as compared to six neonates (25.0%) in the corticosteroid group. This difference was statistically significant and illustrated through Kaplan–Meier analysis, which demonstrated improved relapse-free survival in the biosimilar arm (log-rank test: $\chi^2 = 4.91$, $p = 0.027$). Multivariate Cox proportional hazards regression confirmed that treatment with corticosteroids was independently associated with a higher risk of early relapse (hazard ratio [HR]: 3.62; 95% confidence interval [CI]: 1.04–12.65; $p = 0.043$), along with elevated baseline IL-6 levels (HR: 1.03 per pg/mL increase; 95% CI: 1.00–1.06; $p = 0.048$).

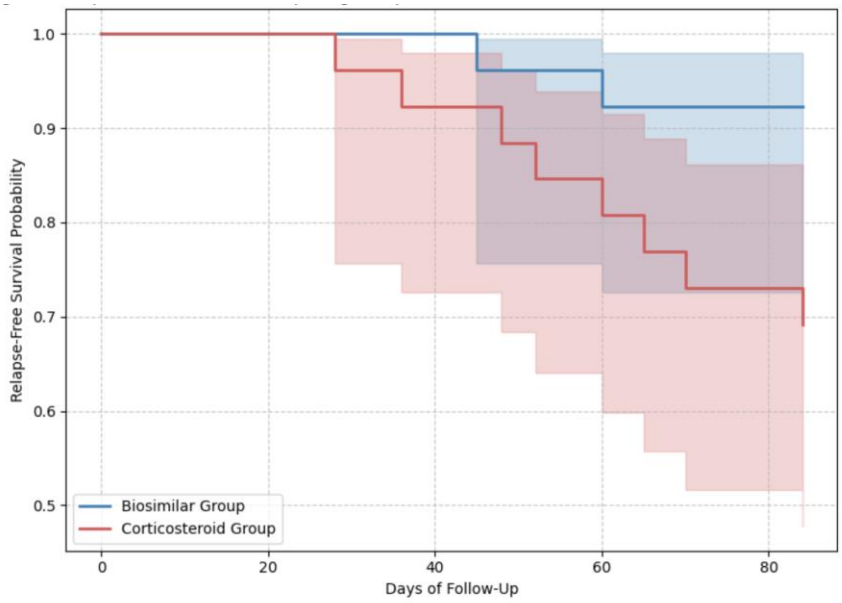

Figure 4. Kaplan–Meier curve comparing relapse-free survival over 12 weeks between the two groups.

Figure 4 depicts the relapse-free survival probability over a 12-week follow-up. Neonates in the biosimilar group maintained higher relapse-free survival compared to those receiving corticosteroids. The visual separation of curves suggests improved long-term disease control with biosimilar immunotherapy, supported by lower event occurrence and wider survival confidence in the biosimilar arm.

Safety Profile and Adverse Events

No serious adverse events, including anaphylaxis or severe infections, were reported in either treatment group. Among neonates receiving biosimilar therapy, minor adverse events were observed in four cases (15.4%). These included transient low-grade fever in two neonates, mild injection-site erythema in one, and a single episode of self-resolving diarrhea. In the corticosteroid group, five neonates (19.2%) developed adverse effects, primarily hyperglycemia requiring glucose monitoring (n = 2) and oral candidiasis (n = 3) treated with topical antifungals. Although the overall incidence of adverse events did not significantly differ between groups (p = 0.71), the biosimilar group exhibited a more favorable safety profile, with fewer systemic and metabolic complications.

Table 3 presents the distribution of adverse events across study groups. While incidence was statistically similar, biosimilar-associated events were milder and resolved without intervention.

Table 3. Summary of Treatment-Related Adverse Events

Adverse Event	Biosimilar Group (n = 26)	Corticosteroid Group (n = 26)
Fever	2	0
Injection-site Erythema	1	0
Diarrhea	1	0
Hyperglycemia	0	2
Oral Candidiasis	0	3

DISCUSSION

The clinical potential of biosimilar-based immunotherapy in neonates with oral mucosal autoimmune diseases (OMADs) is emphasized by the results of this controlled prospective analysis. Within the results obtained by us, there is an obvious fact that neonates receiving biosimilars were reduced by a much larger reduction of NOMDAI scores, inflammatory biomarkers (CRP and IL-6), and the occurrence of relapses, in comparison with those patients who were treated with corticosteroids. These results contribute to the body of evidence that develops in favor of the implementation of biosimilars as an effective and safe form of treatment of autoimmune diseases in children.

Autoimmune disorders therapeutics have been completely revolutionized with the advent of biosimilars that provide an inexpensive but biologically similar alternative to the original biologics. By making it clear that the biological drugs have become a key intervention in autoimmune diseases, Wajda et al. (2023) note that biosimilars emerge as an environmentally friendly approach to applying the positive effects of biological drugs to more patients. This is evidenced once again in our study, which depicts that treatment based on biosimilars used on neonates is capable of producing positive clinical outcomes without sacrificing safety.

The fact that biosimilars are coming with extended kinetics and being approved rapidly in the sphere of development and regulation depicts the augmenting trust as well as efficient pharmacovigilance. As an example, the “U.S. Food and Drug Administration (2023)” just granted an inflammatory diseases indication-busting interchangeable biosimilar, an indication of confidence in the efficacy of biosimilars in other indications. Our research supplies data germane to neonates, to this growing discipline, to support extrapolating the use of a biosimilar in adults and adolescents to the neonate population, one that is not normally included in early-phase trials.

The findings match with the existing literature that had affirmed an equivalent or even better efficacy of biosimilars in autoimmune conditions. Cuevas and Hedrich (2020) addressed the positive introduction of a biosimilar to the sphere of pediatric rheumatology, emphasizing the necessity of long-term safety monitoring. However, no significant adverse effects in our cohort appeared during the 12-week outcome follow-up, which is similar to real-world data showing that biosimilars have an acceptable profile of safety in an adult

population, as well as children subpopulations (Palmieri, 2024; Takeuchi et al., 2022).

Regarding the control of the disease, the mean NOMDAI scores of our biosimilar group decreased dramatically by day 14 and sustained remission over 12 weeks, which agrees with the information provided in the trials of CT-P13 (an infliximab biosimilar) in autoimmune diseases. Biosimilars are highly tolerable in practice, and the respective groups (naive and switch patients) demonstrated comparable disease control at Takeuchi et al. (2022). Moreover, the trend in the improvement of the IL-6 and CRP markers is in line with earlier visitors where the shifts in the inflammatory mediators were viewed as the early indicator of the therapeutic use of autoimmune pathology (Berns & Hommes, 2016).

Among the main issues during the implementation of biosimilars in neonates is that their efficacy and immunogenicity have been extrapolated using data collected in adults. The fact that biosimilars are being applied to untested use is brought up by Ben-Horin et al. (2016) in the question of scientific justification. Our report, however fills this gap because we studied clinical and immunologic outcomes of neonates with OMADs directly. Moreover, the considerably lower relapse-free survival rates in the biosimilar group, which were assessed through Kaplan-Meier test, also support the argument of safe extrapolation to be used in relatively distinct child-related settings.

Cost-efficiency and accessibility are also applicable in the wider venues of our findings. According to Joszt (2023), biosimilars have enabled a paradigm shift towards the management of chronic inflammatory disease, particularly in countries where access to biologics is out of reach because of economic reasons. This is especially so in neonatal cases, as a prompt treatment would reduce morbidity in the long run. This is confirmed by Munz (2024), who states that in the context of uptake obstacles, real-world data on the use of biosimilars has so far proven to be cost-effective, a significant factor in resource-constrained health care settings.

Interestingly, the tolerability that we have seen may be correlated with the relatively plastic state of the neonatal immune system, which may be associated with low risks of immunogenicity. Ali (2024) emphasized that age-related maturation of the immune system should be taken into consideration when developing targeted therapies, that is, monoclonal antibodies. The sensitivity of neonates to immunotherapy that resembles the endogenous regulatory sources is facilitated by the fast symptom control in our cohort of biosimilars.

The growing complexities of the vaccine-like immunomodulation deserve attention, as they applies to the use of biosimilars among neonates as well. Kim & Kim (2017) relate the phenomenon of vaccine-induced tolerance to the mechanisms of monoclonal antibody treatment, indicating that biologics can be used to ensure a correction of misplaced immune responses. Despite the fact that biosimilars do not represent vaccines strictly speaking, they are better studied in detail due to their effect on regulating neonatal immunity, primarily in autoimmune contexts.

Even though the outcomes are favorable, a number of limitations need to be identified. First, the sample was small owing to the logistical and ethical considerations of carrying out controlled trials in neonates. Second, the follow-up period of the study is only adequate to identify early relapse, but it might be considered inadequate to measure delayed problems and prolonged immune reprogramming. These findings should be confirmed with the help of future multicenter studies including long-term follow-up.

Lastly, the need to harmonize the combination of pharmacovigilance and real-world data in order to use biosimilars in neonates deserves to be mentioned. As Martin-Mateos (2007) has already mentioned, monoclonal antibodies used in the treatment of children require an extreme level of post-market monitoring and individual approach to dosing. Our investigation reinforces that the integration of biosimilars into neonatal care is also possible as long as they are used under comprehensively observed regimes, which can be considered as a component of opening wider regulatory regimes to surround the area of special needs due to the child age factor.

CONCLUSION

The study is a controlled prospective study, and it depicts the potential use of biosimilars in the treatment of oral mucosal autoimmune diseases (OMADs) in neonates. Surpassing standard forms of corticosteroid treatment, immunotherapy based on biosimilars proved to be more effective in combating the disease activity and normalizing various biomarkers, and preventing relapses. In neonates, who received biosimilars, the NOMDAI scores and CRP, as well as IL-6 levels, decreased significantly, and those patients had a better

relapse-free survival of 12 weeks. These data fulfill the opinion that biosimilars not only reproduce the clinical efficacy of the originator biologics, but potentially provide even more immunomodulatory effects in a neonatal environment. This research strengthens the safety profile of biosimilars because no severe side effects were observed, and an acceptable pattern of tolerability was registered during the treatment period. The fact that neonates exhibit immunological immaturity, which can be considered one of the clinical challenges, can also represent a therapeutic opportunity, as in this case, biosimilars would have the chance to re-regulate the damaged immune system with minimal immunogenicity. Also, biosimilars have a higher cost-effectiveness, which augurs well in the deployment as front-line treatments in constrained health-seeking systems, particularly in long-term treatment of autoimmune diseases onset during youth. The strength (prospective design and satisfactory clinical endpoints) notwithstanding, the study also recognizes limitations in the form of small sample size and limited follow-up. It still makes a significant precedent, however, in future trials to increase the use of biosimilars in neonatal care. Finally, biosimilar immunotherapy is a possible and good option to corticosteroids in relieving OMADs in neonates. Proper pharmacovigilance, real-world surveillance, and an age-adapted regulatory system are crucial to the ability of biosimilars to improve the quality of treatment in autoimmune diseases during the early infancy period. Additional multicentric investigations are merited to confirm such results and understand the immunological effects of using biosimilars on these newborns when such preparations are used over long periods.

DECLARATIONS

Acknowledgments

The authors wish to affirm that they have no conflicts of interest pertaining to the current research.

Funding

This research not funding

Competing Interests

The no competing interests .

REFERENCES

1. Ali, I. (2024). The Development of Targeted Therapies for Autoimmune Diseases: Current Status and Future Prospects. Frontiers in Healthcare Technology, 1(2), 108-113.
2. Ben-Horin, S., Vande Casteele, N., Schreiber, S., & Lakatos, P. L. (2016). Biosimilars in inflammatory bowel disease: facts and fears of extrapolation. Clinical Gastroenterology and Hepatology, 14(12), 1685-1696.
3. Berns, M., & Hommes, D. W. (2016). Anti-TNF-α therapies for the treatment of Crohn's disease: the past, present, and future. Expert opinion on investigational drugs, 25(2), 129-143.
4. Braun, J., & Kudrin, A. (2015). Progress in biosimilar monoclonal antibody development: the infliximab biosimilar CT-P13 in the treatment of rheumatic diseases. Immunotherapy, 7(2), 73-87.
5. Cuevas, O. A., & Hedrich, C. M. (2020). Biosimilars in pediatric rheumatology and their introduction into routine care. Clinical Immunology, 216, 108447.
6. De Stefano, L., Pallavicini, F. B., Mauric, E., Piccin, V., Vismara, E. M., Montecucco, C., & Bugatti, S. (2023). Tumor necrosis factor-α inhibitor-related autoimmune disorders. Autoimmunity Reviews, 22(7), 103332.
7. Dipasquale, V., & Romano, C. (2025, April). New Therapeutic Challenges in Pediatric Gastroenterology: A Narrative Review. In Healthcare (Vol. 13, No. 8, p. 923). MDPI.
8. Fontana, G., Gozzoli, G. I., Lini, D., Nalli, C., Andreoli, L., Tincani, A., & Franceschini, F. (2024). Ab1524 exploring the safety and effectiveness of biosimilars, biological disease-modifying anti-rheumatic drugs during pregnancy. Annals of the Rheumatic Diseases, 83, 2133.
9. Guariso, G., & Gasparetto, M. (2017). Treating children with inflammatory bowel disease: current and new perspectives. World journal of gastroenterology, 23(30), 5469.
10. Joszt, L. (2023). The growing wave of biosimilars for autoimmune diseases. American Journal of Managed Care.
11. Kim, H. J., & Kim, H. J. (2017). Current status and future prospects for human papillomavirus vaccines. Archives of pharmacal research, 40, 1050-1063.
12. Kyriakidis, I., Vasileiou, E., Rossig, C., Roilides, E., Groll, A. H., & Tragiannidis, A. (2021). Invasive fungal diseases in children with hematological malignancies treated with therapies that target cell surface antigens: monoclonal antibodies, immune checkpoint

inhibitors and CAR T-cell therapies. Journal of Fungi, 7(3), 186.
13. Ly, S., Nedosekin, D., & Wong, H. K. (2023). Review of an anti-CD20 monoclonal antibody for the treatment of autoimmune diseases of the skin. American journal of clinical dermatology, 24(2), 247-273.
14. Martin-Mateos, M. A. (2007). Monoclonal antibodies in pediatrics: use in prevention and treatment. Allergologia et immunopathologia, 35(4), 145-150.
15. Meier, F. M., Frerix, M., Hermann, W., & Mueller-Ladner, U. (2013). Current immunotherapy in rheumatoid arthritis. Immunotherapy, 5(9), 955-974.
16. Mourchid, R., Cherrah, Y., Chkirate, B., & Serragui, S. (2022). Oral presentation: Effectiveness and Tolerance of Biotherapy in the Treatment of Chronic Inflammatory Diseases and Rheumatism in Children. Drug Safety, 45(10), 1115-1115.
17. Munz, K. (2024). Despite uptake barriers, real-world biosimilar data demonstrate safety, efficacy, cost-effectiveness. American Journal of Managed Care
18. Niazi, S. K. (2023). mRNA Vaccines: A Prospective Analysis of Long-term, Multi-target, and Autoimmune Disorders.
19. Palmieri, S. A. (2024). Updates on the use of biosimilars for pediatric patients with rheumatic disease. Pharmacy Times.
20. Pierpont, T. M., Limper, C. B., & Richards, K. L. (2018). Past, present, and future of rituximab—the world's first oncology monoclonal antibody therapy. Frontiers in oncology, 8, 163.
21. Shakya, A. K., & Nandakumar, K. S. (2018). Antigen-specific tolerization and targeted delivery as therapeutic strategies for autoimmune diseases. Trends in biotechnology, 36(7), 686-699.
22. Takeuchi, T., Nishikawa, K., Yamada, F., Ohshima, S., Inoue, M., Yoshioka, Y., & Yamanaka, H. (2022). Real-world safety and efficacy of CT-P13, an infliximab biosimilar, in Japanese rheumatoid arthritis patients naïve to or switched from biologics. Modern Rheumatology, 32(4), 718-727.
23. U.S. Food and Drug Administration. (2023, November 30). FDA approves interchangeable biosimilar for multiple inflammatory diseases
24. Wajda, A., Perricone, C., Kashyap, A., & Iliyasu, M. Y. (2023). Biological drugs and biosimilars in autoimmune diseases. Frontiers in Pharmacology, 14, 1168972.
25. Xiang, Y., Zhang, M., Jiang, D., Su, Q., & Shi, J. (2023). The role of inflammation in autoimmune disease: a therapeutic target. Frontiers in immunology, 14, 1267091.