INTERNATIONAL JOURNAL *of* PEDIATRIC DERMATOLOGY

Official Journal of the World Health Academy of Dermatology and Pediatrics Issue 2 2024

International Journal of Pediatric Dermatology, Vol 1. Iss. 2 (July-December, 2024). ISSN 3035-1006 (online)

Contents

Editorial

The publication of the second issue of the International Journal of Pediatric Dermatology represents a significant milestone for the scientific community engaged in research and clinical practice in pediatric dermatology. Our mission is to provide an excellent platform for sharing innovative studies, relevant case reports, and in-depth analyses that contribute to improving the diagnosis, management, and treatment of dermatological conditions in pediatric patients. Pediatric dermatology is a continuously evolving field, with increasingly complex diagnostic and therapeutic challenges. This second issue of our journal presents a selection of articles that reflect the breadth and depth of research in this field. The included studies offer new diagnostic and therapeutic perspectives, providing a comprehensive view of current scientific knowledge.

In this issue, we have gathered contributions that highlight the evolution of therapeutic and diagnostic strategies for pediatric dermatological diseases.

Among the published works, the case report on the use of hydrotherapy as adjunctive therapy in the treatment of severe pediatric atopic dermatitis stands out. This study demonstrates how the combination of dupilumab and hydrotherapy can significantly improve skin hydration and reduce the incidence of secondary infections, opening new therapeutic perspectives. The integration of complementary therapeutic approaches represents a step forward in the personalized treatment of this chronic condition. The study also analyzes the physiological mechanisms that make hydrotherapy a valid support to pharmacological treatment, offering interesting data on the effect of thermal waters on skin barrier function.

Additionally, we present a case of atypical Kawasaki disease in a child with Down syndrome is reported, a rare condition that poses diagnostic and therapeutic challenges. This case highlights the importance of considering atypical manifestations of Kawasaki disease, particularly in patients with genetic comorbidities, to prevent potentially fatal cardiac complications. The timely management of these cases requires careful clinical evaluation and a multidisciplinary approach. The study provides an overview of the challenges clinicians may face in identifying symptoms that do not fit classic diagnostic criteria, emphasizing the need for constant updates in pediatric rheumatology knowledge.

Another highly relevant contributions are two case reports on rare pediatric dermatological conditions: infantile rosacea and periorificial dermatitis. These cases emphasize the necessity of accurate diagnosis to avoid inappropriate treatments and improve patients' quality of life. Early recognition and targeted treatment of these conditions can reduce the risk of complications and enhance clinical outcomes. The in-depth analysis of triggering factors and therapeutic responses has led to new recommendations for managing these rare but clinically significant conditions.

Finally, a cross-sectional study analyzing the association between Hanifin and Rajka's minor criteria with age and gender in the pediatric population affected by atopic dermatitis. The results highlight how certain clinical signs are more frequent in specific age groups and genders, underscoring the importance of a targeted diagnostic approach. The correct identification of these minor criteria could improve diagnostic accuracy and guide more effective prevention and treatment strategies. The study provides a detailed classification of symptoms and their variations, facilitating the early identification of patients at risk of developing more severe forms of the disease.

We would like to express our gratitude to the authors, reviewers, and all those who contributed to the realization of this second issue. Their commitment and dedication have made possible the publication of high-quality research that will contribute to advancing knowledge in this field. The wide range of topics addressed and the depth of the analyses presented demonstrate the importance of scientific collaboration and innovation in pediatric dermatological practice. We hope that the International Journal of Pediatric Dermatology will become a reference point for pediatric dermatologists and researchers worldwide, promoting the dissemination of knowledge and the improvement of care for young patients. The commitment of our scientific community will be essential to continue developing increasingly effective therapeutic and diagnostic approaches.

Happy reading!

Editor-in-Chief

Ianina Massimo, MD

INTERNATIONAL JOURNAL
of PEDIATRIC DERMATOLOGY

Vol 1. Iss. 2 (July-December, 2024)

Case Report

Hydrotherapy as adjunctive therapy of severe pediatric atopic dermatitis treated with dupilumab

A. M. Mósca-Cerqueira[3], C. Pereira Silva[1], I. C. Soligo Kanaan[3], A. J. P. Faria-Jr[1 2]

[1]Universidade Fundação Oswaldo Aranha, Rio de Janeiro, Brazil
[2]Universidade Federal Fluminense, Niterói, Brazil
[3]Hospital Municipal Jesus, Rio de Janeiro, Brazil

KEYWORDS

atopic dermatitis, dupilumab, hydrotherapy, pediatrics, dermatology

ABSTRACT

Atopic dermatitis (AD) is a chronic inflammatory skin disease with significant morbidity. This report presents the case of a 15-year-old male with severe AD, unresponsive to standard treatments, who showed marked improvement with dupilumab and adjunctive hydrotherapy using Minéraux Beauty Thermal Water™. Over five years of treatment, the patient experienced multiple infections and hospitalizations, with only limited improvement until the introduction of dupilumab and hydrotherapy. The combination therapy resulted in significant lesion resolution and enhanced skin hydration. This case underscores the efficacy of dupilumab as a cornerstone treatment for severe AD and highlights the potential benefits of hydrotherapy as a safe, cost-effective adjunctive therapy. Further research is warranted to explore the synergistic effects of combining immunobiological agents with hydrotherapy in managing severe AD.

CORRESPONDING AUTHOR

Aydamari João Pereira Faria-Jr
VPS, ICHS - Universidade Federal Fluminense
Rua Desembargador Ellis Hermydio Figueira, 783
Bloco A, Sala 212-A
Aterrado, Volta Redonda
RJ - Brazil

aydamari@gmail.com

1. Introduction

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disease and is one of the most common illnesses in children. Its prevalence varies by ethnicity and age group, being approximately 17.6% in Italy, 18.6% in Spain and 20.1% in Brazil (1).

The pathophysiology of AD is not yet fully understood, but it appears to be related to a pathological IgE-mediated Th-2 biased immune response. Several factors seem to play a role in its development, including genetic and environmental factors, as well as altered immune responses, which either directly or indirectly modify the skin barrier, alter its microbiome and lead to the characteristic pruritic lesions (2, 3).

Over 20 genetic variations have been linked to AD, many of which involve the epidermal differentiation complex (EDC). The filaggrin (FLG) gene, a member of this complex, is particularly notable, with loss-of-function mutations being extensively studied in relation to AD (2, 4). Experimental and clinical evidence suggest that these genetic variations, either directly or indirectly, reduce skin hydration, contribute to more pronounced transepidermal water loss (TEWL) and hinder local immune responses. These factors are correlated with the severity of AD lesions and predispose the skin to microbial colonization (5, 6).

Multiple environmental factors may contribute to the pathophysiology of AD. Exposure to air pollution, microorganism colonization, aeroallergens, climate, food allergens and water composition ("hard water") seem to play roles in the pathogenesis of AD (2, 7). Moreover, although not completely understood, interactions between genetic and environmental factors may epigenetically modulate AD physiopathology (8).

In this report, we present the case of a 15-year-old male with severe atopic dermatitis who has been followed for the past five years and only improved after treatment with dupilumab and adjunctive hydrotherapy. The purposes of this report are to reiterate the efficacy of dupilumab in the treatment of severe atopic dermatitis and to highlight the potential benefits of hydrotherapy as a safe and cost-effective adjunctive therapy.

2. Clinical case

A 15-year-old male patient, diagnosed with asthma and atopic dermatitis at the age of three, was first seen in the dermatology department of Jesus County Hospital when he was 10 years old, in 2019. His initial SCORAD (SCORing Atopic Dermatitis) was 56.3. In addition to AD, he presented with toilet seat dermatitis and was treated with multiple medications, including cotrimoxazole, tacrolimus, fluconazole and loratadine.

At age 11, in 2020, his SCORAD was 56.9, and methotrexate, folic acid and risperidone were prescribed. He experienced multiple skin infections, initially treated with clarithromycin and later with amoxicillin and clavulanate. He was subsequently admitted to the hospital for treatment with oxacillin, vancomycin and fluconazole; methotrexate was discontinued. As he began exhibiting depressive behaviors, he started psychotherapy and psychiatric follow up. He was discharged after 14 days of hospitalization.

In 2021, his SCORAD was 62. He was admitted in the hospital once again due to cellulitis and treated with levofloxacin. After discharge, dupilumab was prescribed, but he could not adhere to the treatment due to local and legal distribution issues.

In 2022, he was hospitalized once more due to a severe infection related to his AD and treated with vancomycin, clindamycin and loratadine. He was on escitalopram, fluoxetine and risperidone for his mental health treatment. In 2023, he was prescribed fluvoxamine but discontinued it after approximately six months due to a possible worsening of his skin lesions.

In June of 2023, the patient initiated regular use of dupilumab. Hydrotherapy, using Minéraux Beauty Thermal Water™, was introduced initially through immersion baths, conducted for at least 20 minutes twice daily over seven days. Subsequently, it was used as a topical adjunctive therapy. Following this combined treatment, the patient's lesions exhibited further improvement.

3. Discussion

A comprehensive review of AD and its treatment is beyond the scope of this paper, but some key aspects must be mentioned. AD, especially in its severe form, poses challenges that extend far beyond skin lesions: it impacts patients' psychological and psychiatric health, as well as in their social lives. It also imposes a financial burden, as AD treatment typically involves multiple remissions, complications and infections, which further add to the economic toll on patients and their families (9, 10).

In general, managing severe AD requires a multifaceted approach, including controlling skin inflammation - either topically, systemically or both -, to the elimination (or mitigation) of environmental triggers. All initiatives aim to repair and restore the skin barrier. Treatment should be viewed as a continuum, with behavioral and pharmacological interventions intertwined to reduce both TEWL and local inflammation (11).

Patients should be advised to identify and avoid trigger factors, keep their skin protected and ensure adequate hydration. Suitable moisturizers and creams can help control skin scaling. Baths should be brief and the water should not be too hot. All household cleaning products, including laundry detergents, should be restricted to neutral, fragrance-free detergents; bleach and fabric softeners should also be avoided (3).

Pharmacological interventions include broad action drugs such as corticosteroids, cyclosporine and methotrexate, which reduce the inflammatory cascade dysregulation characteristic of AD physiopathology. Topical corticosteroids are the first-line treatment for AD and are safe and effective when properly used (12).

More targeted immunomodulatory drugs have recently been added to the AD treatment arsenal. Pimecrolimus and tacrolimus are topical options that inhibit calcineurin, leading to reduced secretion of pro-inflammatory cytokines and cellular recruitment (12, 13). Dupilumab, a monoclonal antibody that selectively inhibits IL-4 and IL-13 via a shared subunit receptor, plays a central role in controlling the characteristic AD Th2 skewed immune response. Dupilumab is regarded as the most effective biological treatment for severe AD and is also considered safe for pediatric patients (14, 15).

Adjunctive therapies have historically been used alongside pharmacological therapies in the management of AD. Hydrotherapy is one of the most commonly practiced adjunctive therapies, either in natural settings (e.g. balneotherapy) or topically (16). Despite controversies and difficulties understanding the mechanisms behind the benefits of hydrotherapy and thermal water (17), there is sufficient evidence supporting its benefits as an adjunctive therapy for AD patients (18, 19).

Hydrotherapy can address both AD skin dehydration and the adverse effects of hard water. Thermal and topic waters with specific mineral compositions can reduce TEWL, maintain skin hydration and alleviate AD symptoms. Replacing traditional hard water with softer water (e.g. with lower calcite and dolomite content) has been shown to improve AD severity (20). The benefits of hydrotherapy may also be attributed to its bacteriostatic properties, to its mineral composition, to its non-pathogenic microbiota or a combination of these (16). Overall, hydrotherapy has minimum side effects, is safe and affordable as an adjunctive therapy for AD.

This report presents the case of a 15-year-old boy with severe and refractory AD, characterized by recurrent infections and multiple hospital admissions. Upon his first visit to the Jesus Hospital Dermatology outpatient clinic, at the age of 10, his SCORAD was higher than 50. Despite various treatment approaches and many hospitalizations, his lesions did not improve until he began using dupilumab, alongside a regimen of thermal water adjunctive treatment.

Figure 1 shows the patient's condition before starting dupilumab, and Figure 2 was taken after six months of dupilumab treatment. The dupilumab-mediated improvement is evident, though some AD hallmarks are still present (e.g. dry scaly skin throughout the trunk and legs). Figure 3 illustrates the patient's skin condition after a 7-day immersion hydrotherapy treatment, where noticeable skin hydration and overall improvement were observed.

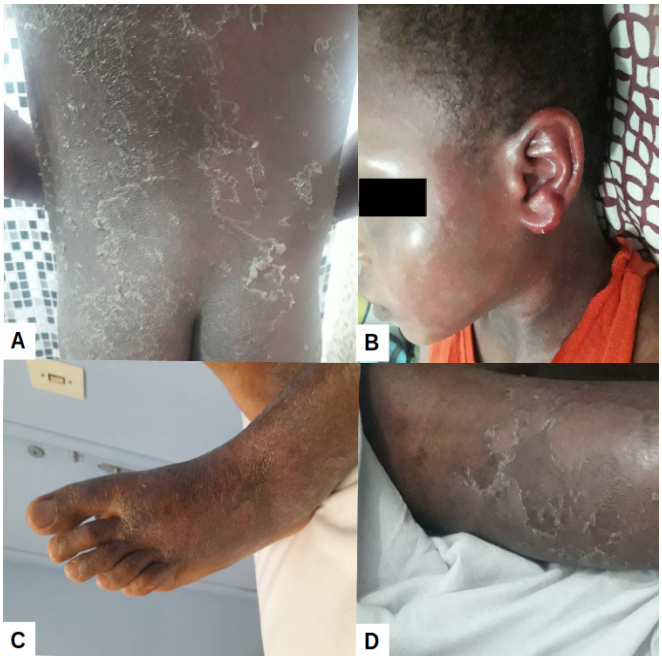

Fig. 1. *Intraepidermal vacuolation with keratohyaline granules. H-E 400x.*

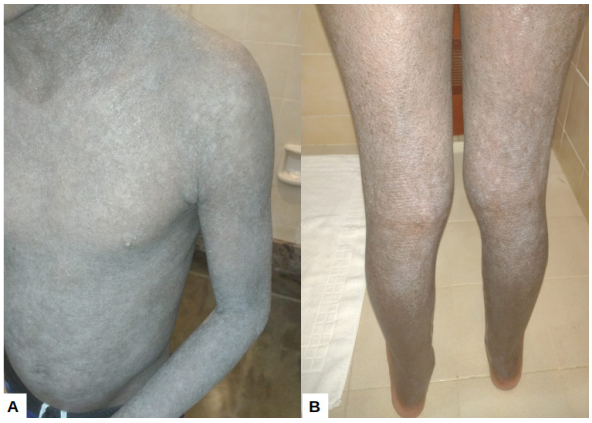

Fig. 2. *Skin appearance after six months of dupilumab treatment and before hydrotherapy.*

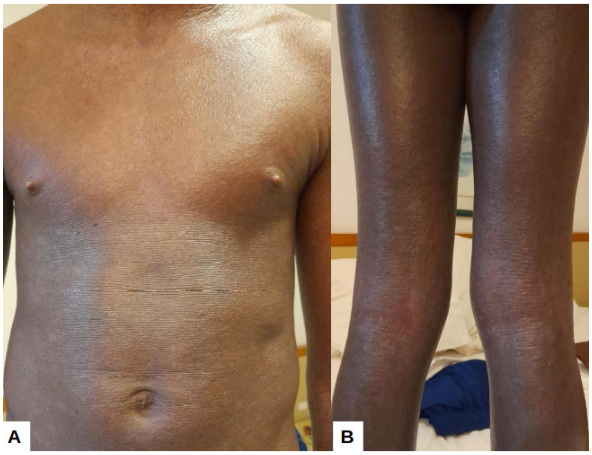

Fig. 3. *Skin appearance after one week of immersion hydrotherapy with Minéraux Beauty Thermal Water™ following six months of dupilumab treatment.*

It is well known that the most appropriate experimental design to evaluate the efficacy of treatments is double-blind randomized controlled trials (RCTs). Nonetheless, case reports can often provide invaluable insights into new or underestimated treatments. Aside from the efficacy of dupilumab treatment, this report also presents the case of a significant potential skin improvement related to the use of hydrotherapy, represented here by Minéraux Beauty Thermal Water™, observed six months after initiating dupilumab.

The mechanisms by which hydrotherapy improves skin lesions are yet to be fully unveiled, but as previously mentioned, as a soft-water treatment, it may contribute to reducing TEWL and skin dehydration, among other mechanisms that are crucial for promoting or accelerating skin healing processes. The association of an immunobiological agent with immunoregulatory properties, such as dupilumab, with hydrotherapy, as represented by Minéraux Beauty Thermal Water™, may have a synergistic effect in the recovery of skin lesions related to severe atopic dermatitis, and more studies are needed to further address the full potential of this association.

4. Conclusion

This report underscores the efficacy of dupilumab in treating severe AD, which remains underreported in the literature. Additionally, it highlights the potential benefits of hydrotherapy as an adjunctive treatment for severe AD. In summary, this report reinforces dupilumab as a safe and effective option for treating severe AD. It also serves as an important preliminary step in exploring the efficacy of high-quality thermal water, represented here by Minéraux Beauty Thermal Water™, as a favorable cost-benefit adjunctive therapy for severe AD lesions, which should be considered in the treatment repertoire for AD.

FUNDING

No funding was received.

DISCLOSURE

All authors report no conflict of interest.

References

1. Silverberg JI, Barbarot S, Gadkari A, Simpson EL, Weidinger S, Mina-Osorio P, et al. Atopic dermatitis in the pediatric population: A cross-sectional, international epidemiologic study. Ann Allergy Asthma Immunol Off Publ Am Coll Allergy Asthma Immunol. 2021; 126(4):417-428.e2.

2. Chong AC, Visitsunthorn K, Ong PY. Genetic/Environmental Contributions and Immune Dysregulation in Children with Atopic Dermatitis. J Asthma Allergy. 2022; 15:1681–700.

3. Wollenberg A, Christen-Zäch S, Taieb A, Paul C, Thyssen JP, De Bruin-Weller M, et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. J Eur Acad Dermatol Venereol. 2020; 34(12):2717–44.

4. Smieszek SP, Welsh S, Xiao C, Wang J, Polymeropoulos C, Birznieks G, et al. Correlation of age-of-onset of Atopic Dermatitis with Filaggrin loss-of-function variant status. Sci Rep. 2020; 10(1):2721.

5. Stevens ML, Zhang Z, Johansson E, Ray S, Jagpal A, Ruff BP, et al. Disease-associated KIF3A variants alter gene methylation and expression impacting skin barrier and atopic dermatitis risk. Nat Commun. 2020; 11(1):4092.

6. Ong PY, Leung DYM. Bacterial and Viral Infections in Atopic Dermatitis: a Comprehensive Review. Clin Rev Allergy Immunol. 2016; 51(3):329–37.

7. Jabbar-Lopez ZK, Craven J, Logan K, Greenblatt D, Marrs T, Radulovic S, et al. Longitudinal analysis of the effect of water hardness on atopic eczema: evidence for gene–environment interaction. Br J Dermatol. 2020; 183(2):285–93.

8. Acevedo N, Benfeitas R, Katayama S, Bruhn S, Andersson A, Wikberg G, et al. Epigenetic alterations in skin homing CD4+CLA+ T cells of atopic dermatitis

patients. Sci Rep. 2020; 10(1):18020.

9. El Achkar Mello ME, Simoni AG, Rupp ML, De Azevedo Simões PWT, De Souza Pires MM. Quality of life of pediatric patients with atopic dermatitis and their caregivers. Arch Dermatol Res. 2023; 315(6):1571–6.

10. Wan J, Mitra N, Hooper SR, Hoffstad OJ, Margolis DJ. Association of Atopic Dermatitis Severity With Learning Disability in Children. JAMA Dermatol. 2021; 157(6):1–7.

11. Aoki V, Lorenzini D, Orfali RL, Zaniboni MC, Oliveira ZNP de, Rivitti-Machado MC, et al. Consensus on the therapeutic management of atopic dermatitis - Brazilian Society of Dermatology. An Bras Dermatol. 2019; 94:67–75.

12. Matthews SJ, Housam N, Lawton S, Taverner P. Atopic eczema in under 12s: diagnosis and management—summary of updated NICE guidance. BMJ. 2023; 382:p1538.

13. Chu DK, Schneider L, Asiniwasis RN, Boguniewicz M, Benedetto AD, Ellison K, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE– and Institute of Medicine–based recommendations. Ann Allergy Asthma Immunol. 2024; 132(3):274–312.

14. Kamal MA, Davis JD, Kovalenko P, Srinivasan K, Simpson EL, Nakahara T, et al. Pharmacokinetics, pharmacodynamics, and exposure–efficacy of dupilumab in adults with atopic dermatitis. Clin Transl Sci. 2022; 15(10):2342–54.

15. Cather J, Young M, DiRuggiero DC, Tofte S, Williams L, Gonzalez T. A Review of Phase 3 Trials of Dupilumab for the Treatment of Atopic Dermatitis in Adults, Adolescents, and Children Aged 6 and Up. Dermatol Ther. 2022; 12(9):2013–38.

16. Galli E, Fortina AB, Ricci G, Maiello N, Neri I, Baldo E, et al. Narrative review on the management of moderate-severe atopic dermatitis in pediatric age of the Italian Society of Pediatric Allergology and Immunology (SIAIP), of the Italian Society of Pediatric Dermatology (SIDerP) and of the Italian Society of Pediatrics (SIP). Ital J Pediatr. 2022; 48(1):95.

17. Cacciapuoti S, Luciano M, Megna M, Annunziata M, Napolitano M, Patruno C, et al. The Role of Thermal Water in Chronic Skin Diseases Management: A Review of the Literature. J Clin Med. 2020; 9(9):3047.

18. Moini Jazani A, Ayati MH, Nadiri AA, Nasimi Doost Azgomi R. Efficacy of hydrotherapy, spa therapy, and balneotherapy for psoriasis and atopic dermatitis: a systematic review. Int J Dermatol. 2023; 62(2):177–89.

19. Figueiredo AC, Rodrigues M, Mourelle ML, Araujo ARTS. Thermal Spring Waters as an Active Ingredient in Cosmetic Formulations. Cosmetics. 2023; 10(1):27.

20. Lopez DJ, Singh A, Waidyatillake NT, Su JC, Bui DS, Dharmage SC, et al. The association between domestic hard water and eczema in adults from the UK Biobank cohort study. Br J Dermatol. 2022; 187(5):704–12.

INTERNATIONAL JOURNAL
of PEDIATRIC DERMATOLOGY

Vol 1. Iss. 2 (July-December, 2024)

Case Report

Exploring the atypical: a case of atypical Kawasaki disease in a 9-year-old Filipino male with Down syndrome

M. R. Piscasio[1], D. J. del Rio[1], E. R. Coo[1]
[1]*Department of Dermatology, Valenzuela Medical Center, Philippines*

KEYWORDS
atypical Kawasaki disease,
incomplete Kawasaki disease,
Down syndrome

CORRESPONDING AUTHOR
Mark Raphael Piscasio,
Department of Dermatology,
Valenzuela Medical Center,
Padrigal St., Karuhatan,
Valenzuela City, 1441,
Philippines

markpiscasio@gmail.com

ABSTRACT
Kawasaki disease (KD) is an acute systemic vasculitis of the small- and medium-sized arteries. Due to its predilection for the coronary arteries, there is a potential for the development of coronary artery aneurysms and subsequent risk of sudden death. Down syndrome is a less-frequently occurring comorbidity in KD, as reported in a Japanese nationwide survey in 2017. A 9-year-old Filipino male with Down syndrome was referred to dermatology service due to generalized erythematous plaques and oral mucosal changes, accompanied with intermittent high-grade fever, and not responding to cefuroxime IV at 64mg/kg/day, paracetamol IV at 10mg/kg, and cetirizine 10mg/day. Further workup revealed dilated right coronary artery on two-dimensional echocardiography. Patient was then managed as a case of atypical Kawasaki disease, and was started on aspirin 80mg/tab ½ tab once daily. It is essential to consider atypical Kawasaki disease in patients having features of KD and yet not meeting the criteria for classic KD and to promptly start proper treatment in order to avoid development of coronary artery aneurysms and subsequent risks. Despite being a less-frequently occurring comorbidity in KD, patients with Down syndrome may also present with incomplete or atypical KD with coronary artery abnormalities.

1. Introduction

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is an acute systemic vasculitis of the small- and medium-sized arteries (1). It is most often seen in children between 6 months and 5 years of age, regardless of ethnicity (2). Given its predilection for the coronary arteries, there is a potential for the development of coronary artery aneurysms and subsequent risk of sudden death (3). According to the registry of the Philippine Pediatric Society, there have been 2,897 reported cases of KD from 2017 to 2020 in the Philippines.

A patient is classified to have atypical or incomplete KD if he or she did not fulfill the clinical diagnostic criteria for classic KD, presenting with symptoms suggestive of KD. Incomplete KD is associated with delayed diagnosis and treatment, which in turn can lead to the development of coronary artery lesions (4). In a 10-year review done in a tertiary hospital in the Philippines, 21% of KD cases presented as atypical or incomplete (5).

Down syndrome, in addition to being the most common chromosomal condition associated with intellectual disability, is characterized by a variety of clinical signs and symptoms (6). In a study determining the prevalence of birth defects at a tertiary level hospital in the Philippines from 2011 to 2014, there were 30 out of 574 neonates born with Down syndrome, with an occurrence of 14.33 per 10,000 births (7).

A Japanese nationwide survey in 2017 reported that Down syndrome is less-frequently occurring comorbidity in KD. According to the survey, in 94,233 patients with KD from 2005 to 2012, only 16 children (0.017%) had Down syndrome, half of which presented with incomplete KD (8). All 16 children with Down syndrome had no coronary artery abnormalities. As Down syndrome is a rare co-morbidity in patients with KD, no studies regarding the incidence of KD among patients with Down syndrome have been published yet.

This report describes a 9-year-old Filipino male with Down syndrome who was managed as a case of Atypical Kawasaki disease, presenting with generalized erythematous plaques, intermittent high-grade fever, and dilated right coronary artery on two-dimensional echocardiography.

2. Clinical case

A 9-year-old Filipino male with Down syndrome was referred to our service due to plaques and pustules on trunk, groin, bilateral upper and lower extremities.

Five days prior to admission, patient had erythematous patches over the groin accompanied with minimal pruritus. No other symptoms were noted. No consult was done and no medications were given.

Four days prior to admission, there was noted spreading of lesions to trunk, and bilateral upper and lower extremities. This was associated with fever (Tmax 39^{o}C), which was intermittently relieved by paracetamol.

Three days prior to admission, patient was brought to a clinic where complete blood count was requested revealing leukocytosis (16.85x10^9/L) with predominance of neutrophils (84%). Patient was given cefuroxime, zinc, and vitamins, which did not provide relief of symptoms. One day prior to admission, there was eruption of pustules over abdomen and groin, and cough, which prompted consult and subsequent admission.

Upon admission, patient was still febrile at 38.6^{o}C. Cardiac examination was unremarkable. Complete blood count was requested showing leukocytosis (17.1x10^9/L) with predominance of neutrophils (75.6%), and lymphocytopenia (18.2%). Patient was started by the main service on cefuroxime IV at 64mg/kg/day, paracetamol IV at 10mg/kg as needed for fever, and cetirizine 10mg/day. Persistence of lesions prompted referral to dermatology service.

Past medical history showed Down syndrome with unrecalled heart disease. He has no known allergies and no prior history of bronchial asthma, pulmonary tuberculosis, and diabetes mellitus. Family, personal, and social history were unremarkable.

On general physical examination, the patient was awake, alert, and afebrile. Examination of the oral mucosa revealed dry lips, and red fissured tongue with prominent papillae (Fig. 1A). No palpable lymphadenopathy was appreciated. Dermatologic examination revealed multiple, generalized, ill-defined, erythematous plaques, some topped with scattered pustules, over the trunk, groin, bilateral upper and lower extremities (Fig. 1B-D). Dermatologic working impression was to consider Kawasaki disease vs. Scarlet fever. Erythrocyte sedimentation rate was normal at 2.0 mm/Hr, C-reactive protein was positive by latex agglutination, and Antistreptolysin O was negative by latex agglutination. Patient was also started on emollient twice daily for the beginning desquamation on the abdomen.

On the seventh day of referral, two-dimensional echocardiography was requested, which showed Congenital heart disease, Tetralogy of Fallot, major aortopulmonary collateral artery, and dilated right coronary artery of 3.0mm (Z score 3.18). Patient was then managed as a case of atypical Kawasaki disease, and was started on aspirin 80mg/tab ½ tab OD. Repeat complete blood count showed normal leukocytes (WBC 7.0 x 10^9/L, neutrophil 47.9%, and lymphocyte 41.0%). He was then discharged stable and improved.

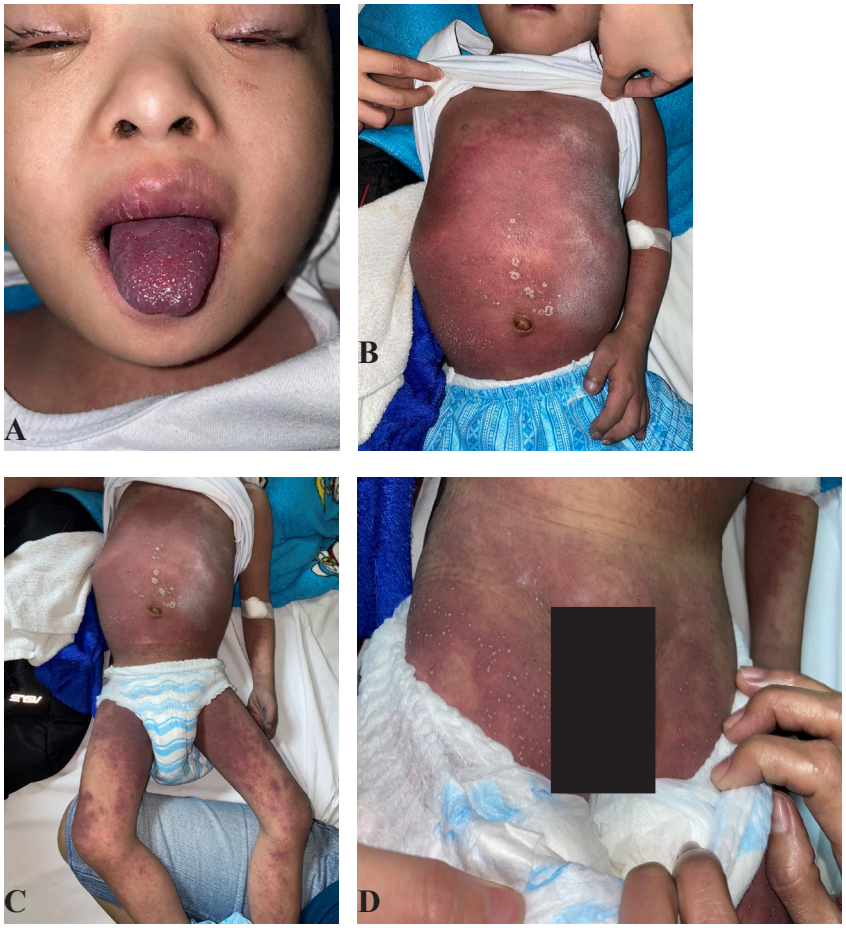

Fig. 1. *(A): Examination of the oral mucosa revealed red fissured tongue with prominent papillae. (B-D): On dermatological examination, there were noted multiple plaques, some topped with scattered pustules, over the trunk, groin, bilateral upper and lower extremities.*

3. Discussion

The etiology of KD is still ambiguous. It has been proposed that an immune response to an infectious organism in a genetically susceptible host is responsible. However, the causative infectious organism has not been identified (9).

The diagnostic criteria for classic KD include fever for at least 5 days accompanied by at least 4 of 5 criteria, as shown in Table I. In our case, the patient presented with 3 of 5 criteria namely: oral mucosal changes, strawberry tongue, erythema of the palms and soles, and scarlatiniform rash.

For patients who do not meet the criteria for classic KD but have no other diagnosis that fits their symptoms, incomplete and atypical forms of KD have been described. According to the 2017 American Heart Association (AHA) scientific statement, incomplete KD is suggested in a patient with at least 5 days of fever, 2 or 3 compatible clinical criteria, and abnormal laboratory values typical of KD or a positive echocardiogram (Z score of left anterior descending coronary artery or right coronary artery ≥2.5; coronary artery aneurysm is observed; or ≥3 other suggestive features exist, including decreased left ventricular function, mitral regurgitation, pericardial effusion, or Z scores in left anterior descending coronary artery or right coronary artery of 2 to 2.5) (10). In our case, the patient presented with

a dilated right coronary artery (Z score 3.16) and the following abnormal laboratory values: positive CRP by latex agglutination, albumin <3.0g/dL, and white blood cell count of >15,000/mm3, confirming the diagnosis of atypical KD.

Table I. Diagnostic criteria of classic Kawasaki disease (10)

Classic KD is diagnosed in the presence of fever for at least 5 d (the day of fever onset is taken to be the first day of fever) together with at least 4 of the 5 following principal clinical features:
1. Erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa
2. Bilateral bulbar conjunctival injection without exudate
3. Rash: maculopapular, diffuse erythroderma, or erythema multiforme-like
4. Erythema and edema of the hands and feet in acute phase and/or periungual desquamation in subacute phase
5. Cervical lymphadenopathy (≥1.5 cm diameter), usually unilateral

Dilated coronary arteries are uncommon as a clinical problem in the pediatric population, including children with Down syndrome. When found, they are usually associated as a sequelae or complication of KD. Tetralogy of Fallot (TOF) is comprised of pulmonary stenosis, overriding aorta, ventricular septal defect, and right ventricular hypertrophy (11). TOF mainly affects the chambers and main arteries, while KD is an acute vasculitis that predominantly affects the coronary arteries (12). In this patient, the coronary artery dilation may be attributed to atypical KD. Coronary arterial lesions have been observed in 5%-20% of patients with KD during the acute stage (13).

The administration of intravenous immunoglobulin (IVIG) and high-dose aspirin has been considered the most appropriate treatment option for patients with KD. These drugs can reduce the development of coronary artery complications when instituted by day 10 of the illness (14). Administration after 10 days of disease onset may help relieve symptoms in patients with active disease, but provides less benefit in reducing coronary artery changes (10). In our case, only aspirin was given to address the diagnosed coronary artery changes on echocardiography, since patient was already stable and asymptomatic.

4. Conclusion

A case of atypical Kawasaki disease with coronary artery abnormality in a 9-year-old filipino male with Down syndrome was presented. It is essential to consider atypical Kawasaki disease in patients presenting with features of KD but not meeting the criteria for classic KD, to promptly start proper treatment and to avoid the development of coronary artery aneurysms and subsequent risks, such as sudden death. Despite being a less-frequently occurring comorbidity in KD, patients with Down syndrome may also present with incomplete or atypical KD with coronary artery abnormalities.

FUNDING

No funding was received.

DISCLOSURE

All authors report no conflict of interest.

References

1) Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. Arerugi 1967; 16:178-222.

2) Hayward K, Wallace CA, Koepsell T. Perinatal exposures and Kawasaki disease in Washington State: a population-based, case-control study. Pediatr Infect Dis J 2012; 31:1027-31.

3) Son MBF, Newburger JW. Kawasaki Disease. Pediatr Rev 2018; 39 (2):78-90.

4) Sudo D, Monobe Y, Yashiro M, Mieno MN, Uehara

R, Tsuchiya K, Sonobe T, Nakamura Y. Coronary artery lesions of incomplete Kawasaki disease: a nationwide survey in Japan. Eur J Pediatr 2012; 171(4):651-6.

5) Chua D, Cueto-Velasco M, Galvez E. A ten-year review of Kawasaki Disease: The Chinese General Hospital experience. PIDSP Journ 1999; Vol.3:6-15.

6) Bull MJ. Down syndrome. New England Journal of Medicine 2020; 382(24):2344-52.

7) Maceda EB, Alcausin MM. Prevalence of birth defects among neonates born at the Philippine General Hospital from 2011 to 2014. Acta Medica Philippina 2017; 51(3).

8) Takatsuki S, Ogata S, Ishii M, Yokozawa M, Ono M, Fujiwara M, Ida H, et al. Low risk of treatment resistance in Down syndrome with Kawasaki disease. Pediatr Int 2017 Dec;59(12):1236-1239.

9) Bayers S, Shulman ST, Paller AS. Kawasaki disease: part I. Diagnosis, clinical features, and pathogenesis. J Am Acad Dermatol 2013; 69(4):501.e1-11.

10) McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, Baker AL, Jackson MA, Takahashi M, Shah PB, Kobayashi T. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. circulation. 2017; 135(17):e927-99.

11) van der Ven JPG, van den Bosch E, Bogers AJCC, Helbing WA. Current outcomes and treatment of tetralogy of Fallot. F1000Res 2019; 8:F1000 Faculty Rev-1530.

12) Freeman AF, Shulman ST. Kawasaki disease: summary of the American Heart Association guidelines. American family physician 2006; 74(7):1141-8.

13) Liu MY, Liu HM, Wu CH, Chang CH, Huang GJ, Chen CA, Chiu SN, Lu CW, Lin MT, Chang LY, Wang JK. Risk factors and implications of progressive coronary dilatation in children with Kawasaki disease. BMC pediatrics 2017; 17(1):1-7.

14) Newburger JW, Takahashi M, Burns JC, Beiser AS, Chung KJ, Duffy CE, et al. The Treatment of Kawasaki Syndrome with Intravenous Gamma Globulin. N Engl J Med 1986; 315:341-7.

INTERNATIONAL JOURNAL
of PEDIATRIC DERMATOLOGY

Vol 1. Iss. 2 (July-December, 2024)

Pediatric periorificial dermatitis and pediatric rosacea: two case reports

A. M. Mósca-Cerqueira[3], C. Pereira Silva[1], C. T. Esteves da Silva Oliveira[1], D. F. de Oliveira[1], P. Guedes Ferreira[4], A. J. P. Faria-Jr[1,2]

[1]Universidade Fundação Oswaldo Aranha, Rio de Janeiro, Brazil
[2]Universidade Federal Fluminense, Niterói, Brazil
[3]Hospital Municipal Jesus, Rio de Janeiro, Brazil
[4]Hospital Municipal Dr. Munir Rafful, Rio de Janeiro, Brazil

KEYWORDS

perioral dermatitis, rosacea, pediatrics, diagnosis, differential

CORRESPONDING AUTHOR

Aydamari João Pereira Faria-Jr
VPS, ICHS - Universidade Federal Fluminense
Rua Desembargador Ellis Hermydio Figueira, 783
Bloco A, Sala 212-A
Aterrado, Volta Redonda
RJ - Brazil

aydamari@gmail.com

ABSTRACT

We present two rare dermatological cases: an 11-year-old boy with pediatric rosacea and a 5-year-old girl with perioral dermatitis. The first patient exhibited central facial lesions that ultimately required hospitalization. He was initially diagnosed with impetigo and treated with cephalexin, oxacillin, and dexamethasone without significant improvement. Subsequent evaluation by a pediatric dermatologist led to a revised diagnosis of pediatric rosacea. The second case involved a 5-year-old girl with periorificial lesions, diagnosed with atopic dermatitis and managed with multiple treatment courses over three years, including corticotherapy, antibiotics and antifungal drugs, without success. The correct diagnosis of periorificial dermatitis was later established, and her condition improved with appropriate therapy. These cases highlight the critical importance of precise dermatological diagnosis to avoid unnecessary and prolonged treatment.

1. Introduction

This report presents two severe pediatric cases of common dermatological conditions: an 11-year-old boy, initially diagnosed with impetigo, later correctly identified as having pediatric rosacea and a 5-year-old girl with a prolonged history of facial lesions ultimately diagnosed with periorificial dermatitis.

Rosacea is a chronic inflammatory disease that manifests in various forms, primarily affecting the central face region. In adults, it is characterized by erythema, telangiectasia, phymatous changes, papules and pustules, according to its subclassifications (1). The exact aetiology and pathogenesis of rosacea are not fully understood, but hypotheses include solar radiation-induced changes and alterations in the expression of immune system elements (e.g., cathelicidins, TLR2, NOD-). The role of microorganisms, particularly the mites Demodex folliculorum and D. brevis, is also considered significant (2–4).

While rosacea predominantly affects adults, with a prevalence of about 5%, it can also occur in children and adolescents. Some studies suggest a pediatric prevalence of around 3% in certain populations. However, the lack of definitive diagnostic criteria may lead to underdiagnosis, leaving the true prevalence in this demographic uncertain (2, 5, 6).

Periorificial dermatitis (POD) is usually a self-limited condition characterized by monomorphic erythematous micropapules, typically distributed around the mouth, nose and eyes (7, 8). Its incidence is not well documented, although it appears to be more frequent among young infants, children and young females - the latter group accounting for 90% of cases (9). The lack of information and consensus regarding its incidence and treatment, especially in pediatrics, may lead to equivocal treatments (10). It was once considered a variant of Rosacea, but it is now recognized as a distinct disorder (11, 12). Its etiology and pathogenesis also remain unknown, but there is an association with the use of corticosteroids (13).

This case series aims to highlight key aspects of the diagnosis and treatment of pediatric rosacea and pediatric periorificial dermatitis, with a particular emphasis on raising awareness of their occurrence in the pediatric population, as these conditions are often overlooked.

2. Case series report

First case

An 11-year-old prepubertal boy, otherwise healthy, presented with facial perinasal lesions that began seven days prior and progressed to hyperemic lesions that extended to the perioral region (Fig. 1a). He sought care at a pediatric emergency room, where he was diagnosed with impetigo and prescribed cephalexin 50 mg/Kg every six hours. After four days of medication, he returned due to worsening symptoms, including purulent facial lesions and difficulty feeding, necessitating hospital admission.

Physical examination revealed extensive erythematous papules distributed periorificially, with no involvement of the periocular region. Oxacillin was initiated at 200mg/kg/day, and laboratory tests, including complete blood count and blood culture, were performed. All results were normal. One day after admission, the lesions developed greenish crusts, prompting the initiation of topical dexamethasone. After four days of hospitalization, he was discharged with a prescription for doxycycline at 100 mg/kg/day, administered orally, and was referred to the pediatric outpatient clinic.

At the outpatient consultation, seven days post-discharge, physical examination revealed erythematous vesiculopapular lesions, alongside candida-like satellite lesions in the frontal region, glabella, and infra-palpebral areas, characterized by erythematous bases and crusty pustules. The patient was subsequently diagnosed with pediatric rosacea. He was then treated with trimethoprim-sulfamethoxazole for 14 days and fluconazole for three days. Following initial improvement, treatment included tacrolimus 0.03%, moisturizer and topical cold chamomile compresses. A multi-repair cream was also prescribed. After 60 days of treatment with tacrolimus 0.03%, azelaic acid 150mg/g and moisturizers, the lesions fully resolved (Fig. 1b).

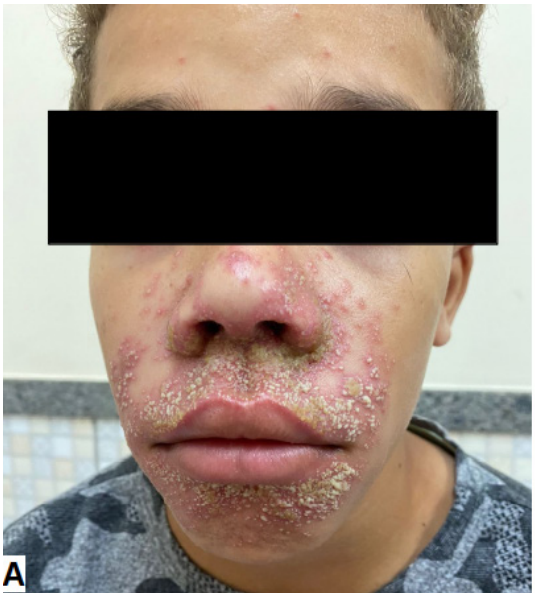

Fig. 1a. *Erythematous vesiculopapular lesions, some coalescing into plaques, with a facial periorificial distribution (eyes, nose and mouth).*

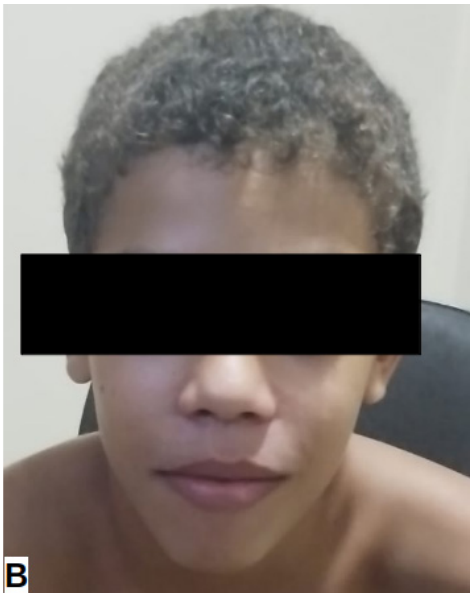

Fig. 1b. *Marked improvement of his lesions after treatment.*

Second case

A 4-year-old girl presented with a one-year history of periorificial lesions, previously diagnosed as atopic dermatitis, and had been treated with various medications (e.g. antibiotics, antihistamines, topical corticosteroids) without improvement. The lesions worsened following a period of mandatory facial mask usage due to COVID-19.

Physical examination revealed periorificial granulomatous papulopustular erythematous lesions, without periocular involvement (Fig. 2a, 2b). She was otherwise healthy, with normal laboratory results, including hemogram, lipid profile and endocrine assessments. Initial treatment included topical metronidazole (7.5mg/g) and moisturizers, followed by topical tacrolimus and azelaic acid. However, over the course of a year, she experienced multiple rhinopharyngeal infections and her facial lesions cycled between improvement and exacerbation. She was treated with amoxicillin/clavulanate and cefadroxil for infections and also with fluconazole and isoconazole for aggravated lesions. Additionally, she developed a strong reaction to topical moisturizers, necessitating the use of topical prednisolone and fluticasone.

Topical metronidazole and ivermectin appeared to worsen her lesions. Ultimately, she was diagnosed with pediatric periorificial dermatitis (POD) and her lesions subsided with a regimen of oral sulfamethoxazole-trimethoprim, combined with topical tacrolimus and azelaic acid. The patient remains under treatment, with her lesions controlled but still experiencing cyclical relapses (Fig. 2c).

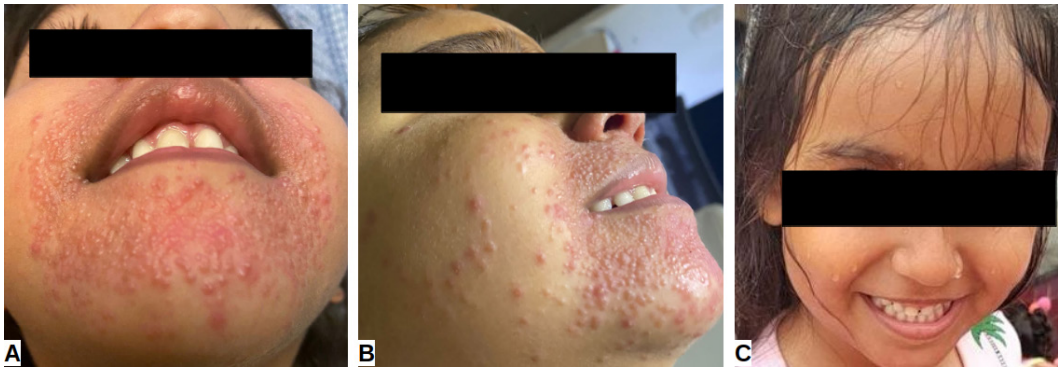

Fig. 2a, b. *Granulomatous papular erythematous lesions, coalescing into extensive plaques in the melolabial fold, extending to periorificial face regions.*
Fig. 2c. *Marked improvement of her lesions after treatment.*

3. Discussion

We have presented here two analogous cases: in the first, a prepubertal boy presented with erythematous papular facial lesions (Fig. 1). Initially diagnosed with impetigo, his condition worsened despite the treatment. The second case involves a 4-year-old girl with extensive erythematous papulopustular lesions in a periorificial distribution (Fig. 2). Initially diagnosed with atopical dermatitis, she did not improve after a year of various treatments.

The resemblance between dermatological lesions can pose significant diagnostic challenges: this report underscores that precise diagnosis and appropriate treatment were achieved only after thorough evaluation. While rosacea and POD are relatively common, their pediatric forms are somewhat rare, with limited literature predominantly consisting of case reports (9, 14). Both conditions present with similar facial erythematous papular lesions, leading to a debate over whether they are distinct disorders of variations of the same condition (2, 11). Their exact diagnosis is not always straightforward and frequently overlooked. A thorough review of all conditions presented is far beyond the scope of this report: our focus is to shed light on both pediatric rosacea and POD so as to raise the awareness of their occurrence.

Despite their similarities, certain key characteristics should be considered to establish an adequate differential diagnosis and treatment in most dermatological lesions. POD and atopic dermatitis, for example, differ significantly in their progression and treatment: POD is often considered self-limited, whereas atopic dermatitis is a chronic disease marked by pruritus, elevated IgE levels and a family history of atopy(15). Impetigo, an acute bacterial infection usually caused by Staphylococcus aureus, differs from rosacea, a chronic condition characterized by waxing and waning cycles (16). Although these conditions may appear similar, their pathogenesis and treatment are distinct.

Rosacea and POD, despite their similarities, have distinguishing features that aid in differential diagnosis. The pathogenesis of both conditions remains poorly understood and treatments generally target the baseline inflammation. This leads to overlapping therapeutic strategies, such as the use of topical metronidazole, azelaic acid, ivermectin and oral antibiotics such as doxycycline, tetracycline and, eventually, in more severe cases, isotretinoin (11, 17, 18). However, the avoidance of corticosteroids is particularly critical in managing POD, where their cessation can be crucial (12). While both conditions in adults are treated similarly, there is limited data regarding pediatric subtleties and most data comes from case reports (3, 19).

4. Conclusion

The cases presented highlight the complexities of pediatric dermatology and underscore the necessity of comprehensive clinical investigations. In the pediatric dermatology setting, it is crucial to consider pediatric POD and rosacea. A thorough evaluation and scrutiny are essential for accurate diagnosis. Finally, it is important to recognize that these dermatological conditions often have impacts extending beyond the skin, particularly in children and adolescents. These aspects, sometimes perceived as peripheral, are significant and should not be underestimated, as they can profoundly affect social and mental health (20).

FUNDING

No funding was received.

DISCLOSURE

All authors report no conflict of interest.

References

1. Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, et al. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. J Am Acad Dermatol. 2018; 78(1):148–55.

2. Hampton PJ, Berth-Jones J, Duarte Williamson CE, Hay R, Leslie TA, Porter I, et al. British Association of Dermatologists guidelines for the management of people with rosacea 2021. Br J Dermatol. 2021; 185(4):725–35.

3. Noguera-Morel L, Hernández-Martín A, Torrelo A. Childhood rosacea and related disorders. Clin Exp Dermatol. 2021; 46(3):430–7.

4. Rosacea: Pathogenesis, clinical features, and diagnosis - UpToDate [Internet]. [cited 2023 Dec 19]. Available from: https://www.uptodate.com/contents/rosacea-pathogenesis-clinical-features-and-diagnosis?search=rosacea&source=search_result&selectedTitle=3~124&usage_type=default&display_rank=2

5. Chen Q, Tang Y, Shi X, Yang X, Shan S, Wang X, et al. Prevalence, clinical characteristics and health-related quality of life of rosacea in Chinese adolescents: a population-based study. J Eur Acad Dermatol Venereol JEADV. 2020; 34(11):e737–9.

6. Gether L, Overgaard LK, Egeberg A, Thyssen JP. Incidence and prevalence of rosacea: a systematic review and meta-analysis. Br J Dermatol. 2018; 179(2):282–9.

7. Fakih A, Makhoul R, Grozdev I. Childhood granulomatous periorificial dermatitis: case report and review of the literature. Dermatol Online J. 2020; 26(12):13030/qt9114v42g.

8. Al-Qassabi AM, Al-Busaidi K, Al Baccouche K, Al Ismaili A. Granulomatous Periorificial Dermatitis in an Adult: A case report with review of literature. Sultan Qaboos Univ Med J. 2020; 20(1):e100–3.

9. Kellen R, Silverberg NB. Pediatric periorificial dermatitis. Cutis. 2017; 100(6):385–8.

10. Gray NA, Tod B, Rohwer A, Fincham L, Visser WI, McCaul M. Pharmacological interventions for periorificial (perioral) dermatitis in children and adults: a systematic review. J Eur Acad Dermatol Venereol JEADV. 2022; 36(3):380–90.

11. Lee GL, Zirwas MJ. Granulomatous Rosacea and Periorificial Dermatitis: Controversies and Review of Management and Treatment. Dermatol Clin. 2015; 33(3):447–55.

12. Lucas CR, Korman NJ, Gilliam AC. Granulomatous Periorificial Dermatitis: A Variant of Granulomatous Rosacea in Children? J Cutan Med Surg. 2009; 13(2):115–8.

13. Searle T, Ali FR, Al-Niaimi F. Perioral dermatitis: Diagnosis, proposed etiologies, and management. J Cosmet Dermatol. 2021; 20(12):3839–48.

14. Kroshinsky D, Glick SA. Pediatric rosacea. Dermatol Ther. 2006; 19(4):196–201.

15. Mortz CG, Brockow K, Bindslev-Jensen C, Broesby-Olsen S. It looks like childhood eczema but is it? Clin Exp Allergy J Br Soc Allergy Clin Immunol. 2019; 49(6):744–53.

16. Hall LM, Gorges HJ, van Driel M, Magin P, Francis N, Heal CF. International comparison of guidelines for management of impetigo: a systematic review. Fam Pract. 2022; 39(1):150–8.

17. Van Zuuren EJ, Fedorowicz Z, Carter B, Van Der Linden MM, Charland L. Interventions for rosacea. Cochrane Skin Group, editor. Cochrane Database Syst Rev. 2015; 2015(4):CD003262.

18. Zhang H, Tang K, Wang Y, Fang R, Sun Q. Rosacea Treatment: Review and Update. Dermatol Ther. 2021; 11(1):13–24.

19. Kellen R, Silverberg NB. Pediatric rosacea. Cutis. 2016; 98(1):49–53.

20. Egeberg A, Hansen PR, Gislason GH, Thyssen JP. Patients with Rosacea Have Increased Risk of Depression and Anxiety Disorders: A Danish Nationwide Cohort Study. Dermatology. 2016; 232(2):208–13.

INTERNATIONAL JOURNAL
of PEDIATRIC DERMATOLOGY

Vol 1. Iss. 2 (July-December, 2024)
ISSN 3035-1006 online

Observational Study

A cross-sectional study to assess the association of minor criteria of Hannifin and Rajka with age and gender in pediatric Atopic Dermatitis population

G. Bansal[1], R. Bansal[2]

[1] Department of Dermatology & STD, F.H Medical College, Agra, Uttar Pradesh, India
[2] Department of Pediatrics, FHMC, Agra, Uttar Pradesh, India

KEYWORDS

Atopic dermatitis, Hannifin and Rajka criteria

CORRESPONDING AUTHOR

Garima Bansal MD,
Assistant Professor,
Department of Dermatology & STD, F.H Medical College, (affiliated with Government of Uttar Pradesh), Agra, Uttar Pradesh, India
drgarimabansal2011@gmail.com

Atopic dermatitis is a chronic relapsing dermatitis characterized by intense itching. Hanifin and Rajka criteria is the most commonly used diagnostic criteria in hospital setup, consisting of 4 major and 23 minor criteria. To estimate the frequency of distribution of Hanifin and Rajka minor criteria in the pediatric age group. To assess the association of age with minor criteria of AD. To assess the association of gender with minor criteria of AD. A cross-sectional study of 150 pediatric patients (≤16 years) was conducted in the Department of Dermatology, who were diagnosed with AD based on history, clinical and ophthalmological examination. Serum IgE was also assessed. The age and gender analysis were done using a chi-square test. The most common clinical features were orbital darkening 133(88.7%), Dennie-Morgan infraorbital fold 126(84%), xerosis 102(68%), keratosis pilaris 101(67.3%), hyperlinear palm 98(65%). Serum IgE was elevated at 26%. The majority presented with high readings with no obvious keratoconus. Male children (88%) presented predominantly with orbital darkening (90.9%) and had an exacerbation in winters (18.2%) in comparison to females (62%) p≤0.05. Children > 1 year (141%) presented mostly with keratosis pilaris (71.6%), non-specific hand-foot dermatitis (49.6%), and facial erythema (34.8%) than in infants (9%) p≤0.05. Minor criteria are useful for the diagnosis of AD. Male children are more affected and manifest with orbital darkening with Dennie -Morgan infraorbital fold as the chief clinical finding in both groups. Factors such as ethnic/racial, environmental, and diet have a role in AD.

1. Introduction

Atopic dermatitis (AD) is a chronic or chronically relapsing hypersensitive manifestation of the skin with itching as a predominant feature. AD constitutes 28.46% of all pediatric dermatoses in pediatric dermatology and is the most common dermatosis registered in children (1). The prevalence of AD in our hospital is 5%. This is due to the variation of the prevalence of clinical features and intensity of AD symptoms with genetic background, climate, geographical regions, food habits, socioeconomic status, availability of healthcare facilities, and others (2, 3). These factors led Hanifin and Rajka to propose a criterion commonly known as "Hanifin and Rajka's diagnostic criteria for AD" (4). Indian literature in research on epidemiology, etiopathogenesis and management of AD is not robust. The overall hygiene being poor and various infections in childhood being rampant in India, AD is less prevalent and less severe. However, in the last four decades, there has been rapid urbanization and improved lifestyle taking place in emerging India that may lead to increased prevalence of AD, if the role of hygiene hypothesis in the pathogenesis of AD is valid and is to be believed (5, 6).

2. Objectives

1. To estimate the frequency of distribution of Hanifin and Rajka minor criteria in the pediatric age group.

2. To assess the association of age with minor criteria of AD.

3. To assess the association of gender with minor criteria of AD.

3. Materials and methods

A cross-sectional study of 150 pediatric patients under 17 years was conducted for 6 months from 20th December 2023 to 19th June 2024, newly diagnosed with AD based on history, clinical and ophthalmological examination. Serum IgE was also assessed.

In every patient, a detailed history concerning the present age, age of onset of the disease (early age of onset was defined as the onset of symptoms of eczema before the age of 5 years, similar to Nagaraja et al. (7, 8), a tendency toward cutaneous infections (described as the presence of at least two episodes of folliculitis/furunculosis/impetiginisation or diagnosed herpes simplex infection in the past 1 year) and nonspecific hand/foot dermatitis (defined as the presence of itchy lesions on one or both hands/feet with erythema and papules/vesicles or scaling, with or without oozing, crusting, fissures, or lichenification), recurrent conjunctivitis, itch when sweating, intolerance to wool and lipid solvents, food hypersensitivity, and influence of environmental and/or emotional factors on the course of the disease was obtained from the parents. Clinical examination was done to record the presence of xerosis, ichthyosis, palmar hyperlinearity (defined by the presence of more than 5 prominent lines longer than 1 cm running across the palm, similar to Böhme et al.) (8), keratosis pilaris (more than 20 follicular, keratotic papules involving at least posterolateral aspects of upper arms or thighs) (8), nipple eczema, cheilitis, Dennie–Morgan infraorbital folds (defined as present when at least one of the infraorbital creases running laterally crossed the pupillary midline, as described by Mevorah et al. (9) orbital darkening, facial pallor or erythema (facial erythema was defined as erythema over cheeks without papules/scaling and facial pallor as skin pallor which is often accentuated peri nasally and/or periorally), pityriasis alba, anterior neck folds (defined as prominent horizontal skin crease(s) on the anterior aspect of the neck, when head is upright), perifollicular accentuation (defined as dermatitis enhanced around hair follicles in ≥2 areas with a diameter >5 cm) (8), and white dermographism. Ophthalmological evaluation to see for the presence of keratoconus and anterior subcapsular cataract was performed by an ophthalmologist. Blood test to assess serum immunoglobulin E (IgE) level was conducted at the laboratory.

4. Statical analysis

Data was entered into the Microsoft Excel software (Window-10). Frequency, percentage, mean, and standard deviation were calculated. The Bar diagram and multiple bar diagram were prepared. A chi-square test was applied. The P-value was judged at 5% level of significance. Jamovi software was used for the test of significance.

5. Results

A total of 150 children were enrolled in the study; of these 88 were males and 62 were females. The mean age was 5.63(SD±3.21) years as shown in Table I.

Table I. Baseline characteristics of the participants.

Characteristics	**Statistics (Measure)**	
Age	Mean ± sd (Rang)	5.63±3.21 (1-15)
Gender	Females (%)	62 (41.3%)
	Males (%)	88 (58.7%)

The distribution of clinical features of minor criteria of Hannifin and Rajka is shown in Table II and Figure 1 the most common features were orbital darkening (88.7%), Dennie-Morgan infraorbital fold (84%), xerosis (68%), keratosis pilaris (67.3%), hyper linear palm (65%), facial pallor (63.3%), pityriasis alba (60.7%.), winter variation was seen more frequently (52.7%) than in summer exacerbation (26%), cheilitis (52%), itching when sweating (52%), tendency for cutaneous infection (48%), prominent anterior neck fold (48%), non-specific hand feet dermatitis (47.3%), perifollicular accentuation (45.3%), facial erythema (37.3%), intolerance to wool and lipid solvent (17.3%). Serum IgE was elevated in 56.7%. Eye symptoms (1.3%), recurrent conjunctivitis (2.7%), nipple eczema (0.7%), white dermographism, and food hypersensitivity were not observed. High reading was observed in (2.7%) with suspect keratoconus in (2%) children. No obvious keratoconus was seen.

Table II. Distribution of minor criteria (percentage values).

Minor Criteria	**Frequency**	**Percentage**
Early age of onset	43	28.7
Tendency for cutaneous infections	72	48
Tendency to nonspecific hand/ foot dermatitis	71	47.3
Xerosis	102	68
Ichthyosis	92	61.3
Hyperlinear palms	98	65.3
Keratosis pilaris	101	67.3
Nipple eczema	1	0.7
Cheilitis	78	52
Dennie-Morgan infraorbital fold	126	84

Recurrent conjunctivitis		4	2.7
Course influenced by environmental factors- Winter / Summer	**Summer**	39	26
	Winter	79	52.7
	No variation	32	21.3
Orbital darkening		133	88.7
Facial Pallor		95	63.3
Facial Erythema		56	37.3
Pityriasis alba		91	60.7
Anterior neck folds		72	48.0
Perifollicular accentuation		68	45.3
Itch when sweating		78	52.0
Intolerance to wool and lipid solvents		26	17.3
Food hypersensitivity		0	0.0
White dermographism		0	0.0
Eye symptoms		2	1.3
Serum IGE		85	56.7
High reading (keratoconous)	high reading with suspect keratoconous	3	2.0
	high reading	4	2.7
	Normal	143	95.3

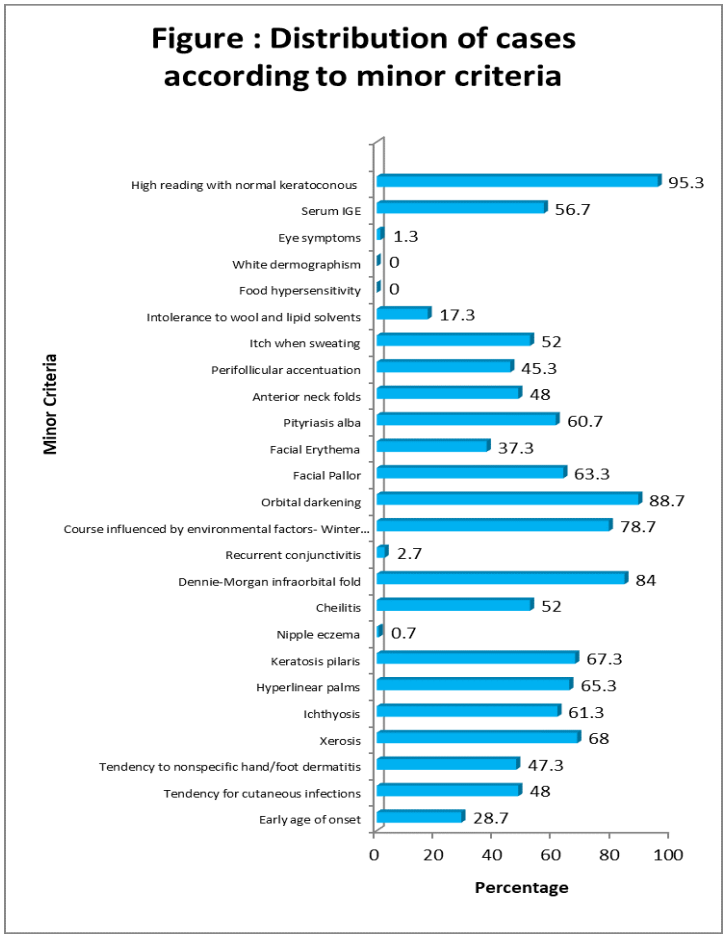

Fig. 1. *Percentage distribution of study of participants according to minor criteria.*

In our study, male children (88%) were more affected than female children as shown in Figure 2. Males presented predominantly with orbital darkening (90.9%), Dennie-Morgan fold (83%), xerosis (70.5%), ichthyosis (69.3%), keratosis pilaris (68.2%), facial pallor (65.9%), pityriasis alba (62.5%), winter exacerbation was observed in (60.2%) in comparison to summer (18.2%). Serum IgE was raised in 58% and 4 male children had high reading and 1 male child and 2 female children had high reading with suspect keratoconus. Photographs of numular dermatitis, facial dermatitis and pityriasis alba is shown below (Figures 3, 4, 5).

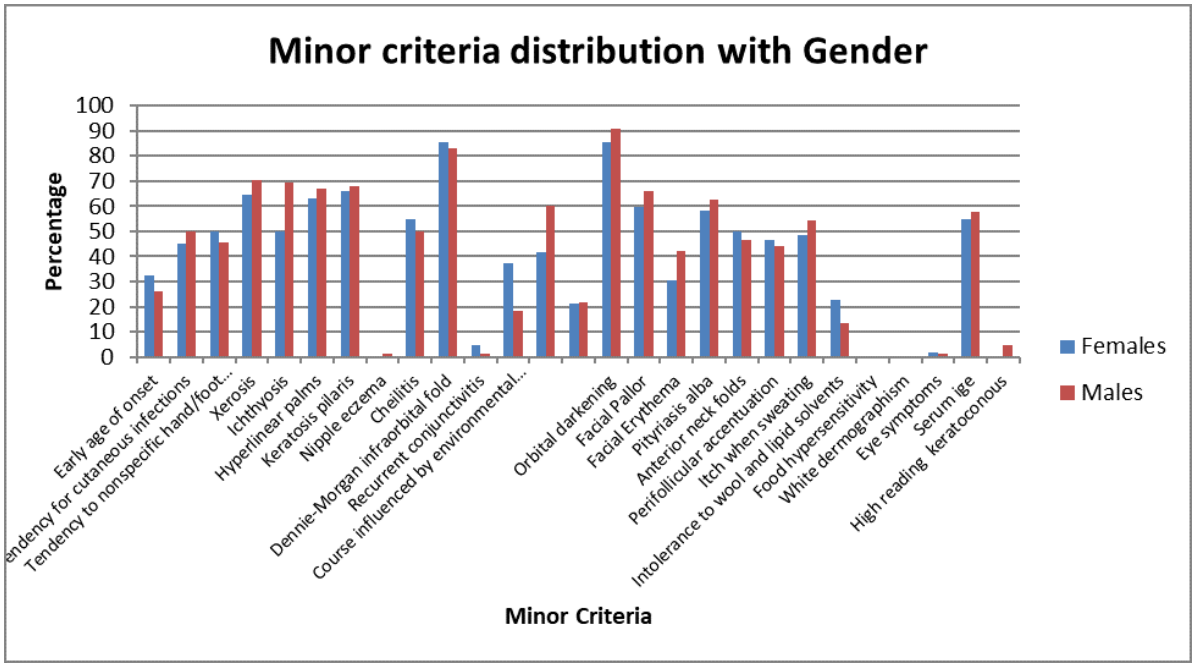

Fig. 2. *Gender-wise distribution of minor criteria.*

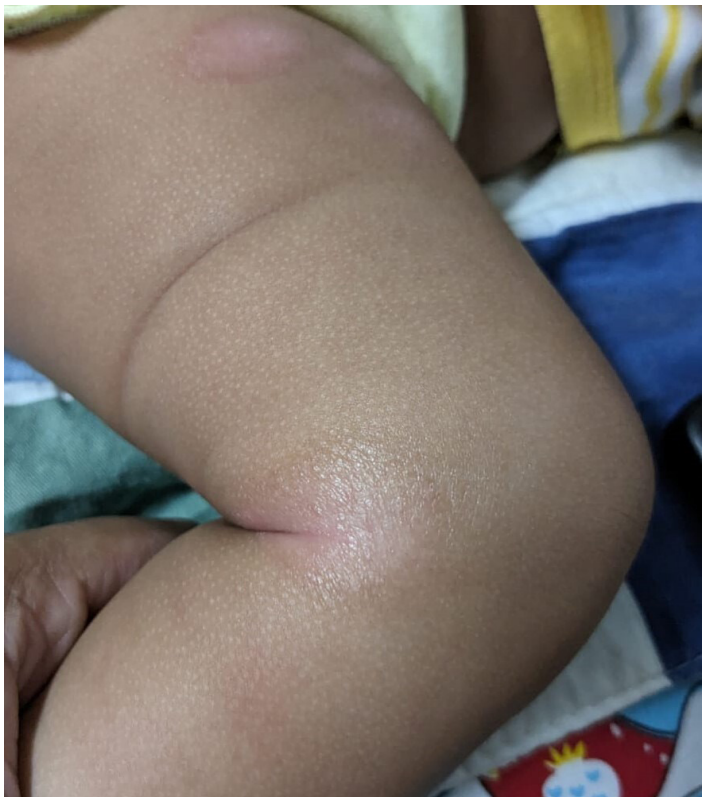

Fig. 3. *Photograph showing perifollicular accentuation and Nummular dermatitis.*

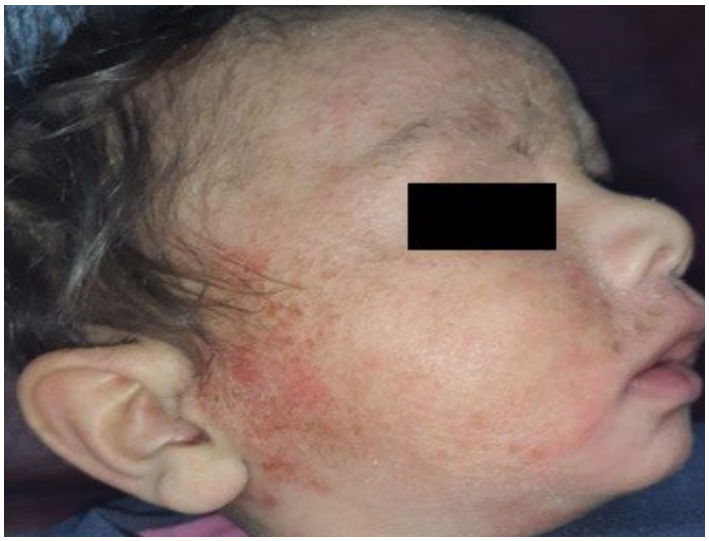

Fig. 4. *Photograph showing facial dermatitis.*

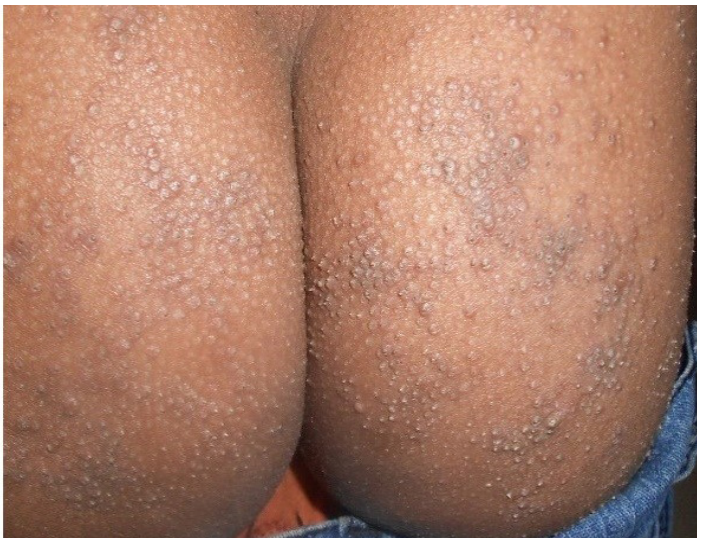

Fig. 5. *Photograph showing Keratosis Pilaris.*

One hundred forty-one children were > 1 year, as depicted in (Table III) and presented with orbital darkening (88.7%) and Dennie-Morgan fold (84.4%), keratosis pilaris (71.6%), xerosis (67.4%), hyperlinear palms (66%) and facial erythema (64.5%). Serum IgE was raised in 81 (57.4%) children. Ophthalmological examination revealed "high reading error" was seen in 4 children and "high reading error with suspect keratoconus" in 3 children.

Table III. Association of minor criteria with Age Group.

Minor criteria	**≤1 year n=9 (%)**	**>1 year n=141 (%)**	**P value**
Early age of onset	4(44.4)	39(27.7)	0.280
Tendency for cutaneous infections	2(22.2)	70(49.6)	0.110
Tendency to nonspecific hand/foot dermatitis	1(11.1)	70(49.6)	0.025
Xerosis	7(77.8)	95(67.4)	0.517
Ichthyosis	8(88.9)	84(59.6)	0.080

Hyperlinear palms		5(55.6)	93(66.0)	0.525
Keratosis pilaris		0(0.0)	101(71.6)	0.00*
Nipple eczema		0(0.0)	1(0.7)	0.800
Cheilitis		5(55.6)	73(51.8)	0.826
Dennie-Morgan infraorbital fold		7(77.8)	119(84.4)	0.599
Recurrent conjunctivitis		0(0.0)	4(2.8)	0.609
Course influenced by environmental factors- Winter / Summer	**Summer**	4(44.4)	35(24.8)	0.398
	Winter	4(44.4)	75(53.2)	
	No Variation	1(11.1)	31(22.0)	
Orbital darkening		8(88.9)	125(88.7)	0.983
Facial Pallor		4(44.4)	91(64.5)	0.225
Facial Erythema		7(77.8)	49(34.8)	0.010*
Pityriasis alba		5(55.6)	86(61.0)	0.746
Anterior neck folds		3(33.3)	69(48.9)	0.364
Perifollicular accentuation		2(22.2)	66(46.8)	0.151
Itch when sweating		4(44.4)	74(52.5)	0.640
Intolerance to wool and lipid solvents		2(22.2)	24(17.0)	0.689
Food hypersensitivity		0(0.0)	0(0.0)	-
White dermographism		0(0.0)	0(0.0)	-
Eye symptoms		0(0.0)	2(1.4)	0.719
Serum IgE		4(44.4)	81(57.4)	0.445
High reading (keratoconus)	**high reading with suspect keratoconus**	0(0.0)	3(2.1)	0.791
	high reading	0(0.0)	4(2.8)	
	normal	9(100.0)	134(95.0)	

6. Discussion

Atopic Dermatitis is one of the most common eczematous conditions presenting in the childhood age group because of rapid urbanization. The change in environment, food habits, lifestyle and hygiene contribute to its early onset. For the diagnosis of Atopic Dermatitis, a lot of criteria have been proposed like Hanifin and Rajka's criteria, U. K. diagnostic criteria (William et al., 1994), and ISAAC (International Study of Asthma and Allergies in Childhood) questionnaire (1995) but of all these Hanifin and Rajka's criteria have been validated the most (3). The mean age for the presentation of clinical features of AD children was 5.63(±3.21) years. A similar finding was observed in the studies conducted by Dhar et al. and Nagaraja et al., on children

aged 3 months to 12 years, in which it was 4.37 ± 3.42 years and 4.04 ± 3.42 years, respectively (5, 6, 7).

The most common finding in the minor criteria of AD was periorbital darkening (88.7%) and Dennie Morgan infraorbital fold (84%) analogous with other findings by Nagaraja et al and Kanwar AJ and Parthasarathy N et al. followed by xerosis 68% keratosis pilaris 67.3% and hyperlinear palms 65.3% as also observed by Kanwar et al. (7, 10, 11). Other findings of minor features like perifollicular accentuation (45.3%) and pityriasis alba (60.7%) were also observed comparable to the findings of the aforementioned authors.

Hand eczema was quite common in the childhood group; 47.3% of the childhood AD patients had hand eczema. The corresponding figures in Dhar and Kanwar's study were 13.64% and 4.29%, respectively (5, 10).

Out of 150 cases in our study, 79 of the cases gave a history of exacerbation of the lesions during the winter season, 39 gave a history of summer exacerbation and 32 had no seasonal variation. This is similar to other studies conducted in northern and eastern parts of India where winter and summer exacerbations are comparatively higher (6, 7, 11, 15).

Criteria such as nipple eczema, recurrent conjunctivitis, food hypersensitivity, and white dermographism were not observed in any of the 150 cases in our study. Nagaraja et al. and Sarkar et al. also noted similar findings. Kanwar et al. did not find any significance of nipple eczema, white dermographism, and recurrent conjunctivitis (10). Nipple eczema was found to be nonspecific in a study by Nagaraja et al. (7).

In our study, a history of intolerance to wool lipid solvents was present in 17.3% in contrast to Nagaraja et al. where it was observed in 41% and Kanwar et al reported in 28% This could be attributed to less exposure of woolens (5, 7, 10).

The serum IgE was raised in 68.7% which was consistent with the report by Nagaraja et al, Dhar et al., Kanwar Agarwal et al. (5,7,10,12).

In a study of 100 patients, 43% had findings in their eyes (17). Of these, 41.9% had involvement of the eyelids, 37.2% had conjunctival involvement, and the rest had involvement of both. Eye changes like isolated blepharitis, loss of the eyelashes, eczema of the eyelids, and conjunctival papillae were observed. In contrast to our study, eye symptoms were 1.1%, which can be explained by that, the cases in the previous studies resort to repeated rubbing leading to infections.

Anterior subcapsular cataract and keratoconus, the minor features for diagnosis of AD, in Hanifin and Rajka's criteria were not found in any patient. Features predisposing a patient for eye involvement are family history of atopy, palmar hyperlinearity, dryness of the skin and Dennie Morgan folds.

Ocular examination to diagnose keratoconus and anterior subcapsular cataract were performed by ophthalmologists, in our hospital. In 126 out of 150 cases, ophthalmological examination was done and 24 were non-compliant, being less than 2 years of age. Anterior subcapsular cataract was not observed among any of the children examined. "High reading but no obvious keratoconus" was noted in 4 cases, while 3 cases were labeled as "keratoconus suspect". The parents of these seven children were advised to follow up once in 6 months for an ophthalmological examination of their child. "Keratoconus suspect" is defined by the presence of asymmetric bowtie/skewed radial axes pattern on video keratography in the absence of slit-lamp findings or scissoring on retinoscopy (13). Nagaraja et al. in their study did not observe keratoconus or anterior subcapsular cataract in any of the patients (7). Keratoconus is postulated to arise due to chronic rubbing of the eyes in AD patients (14).

A higher prevalence was seen in males as compared to females (1.5:1). Similar results were observed in other Indian studies such as Nagaraja et al., (7) Kanwar et al. (10) and Dhar et al. (5) However, in Parthasarathy et al. [11] there was almost equal distribution among both genders (25%). The males presented predominantly with ichthyosis in 69.3% and females 50% (p=0.017).

The onset of symptoms of AD was seen in infant group 44.4%, is consistent with the finding of Shetty et al. (16). The children presented with a tendency to non-specific hand/foot dermatitis 49.6% in compari-

son to infants 11.1%(p=0.025), keratosis pilaris 71.6% children and no infants (p=0.0) and facial erythema infant 77.8% and 34.8% in children (p=0.010).

No correlation between facial eczematous lesions and eye changes was observed in contrast to earlier published studies. The authors explained this by the absence of habitual rubbing to relieve itching which is considered to be responsible for changes in and around the eyes (5).

7. Limitation

This was a single-centre study. In addition, the invasive minor criteria were not studied.

8. Conclusion

From the above discussion, it is evident that the prevalence and severity of AD are influenced by factors such as ethnic/racial factors, climate, geographical regions, food habits, and socioeconomic status. Therefore, dermatologists should know common clinical features of AD in a given population to diagnose the condition and thereby provide treatment to reduce morbidity along with appropriate counselling.

FUNDING

No funding was received.

DISCLOSURE

All authors report no conflict of interest.

INFORMED CONSENT

Informed consent was obtained from the parents of the children included in this case report.

References

1. Sinha PK. Clinical profile of infantile atopic eczema in Bihar. Indian J Dermatol Venereal Leprol. 1972; 38:179–84.

2. Karthikeyan K, Thappa DM, Jeevankumar B. Pattern of pediatric dermatoses in a referral center in South India. Indian Pediatr. 2004; 41:373–7.

3. Brenninkmeijer EE, Schram ME, Leeflang MM, Bos JD, Spuls PI. Diagnostic criteria for atopic dermatitis: A systematic review. Br J Dermatol 2008; 158:754-65.

4. Ardern-Jones MR, Flohr C, Reynolds NJ, Holden CA. Atopic eczema. In: Griffiths CE, Barker J, Bleiker T, Chalmers R, Creamer D, editors. Rook's Textbook of Dermatology. 9th ed Vol. 41. Oxford: Blackwell Publishing 2016. p. 1-41, 34.

5. Dhar S, Kanwar AJ. Epidemiology and clinical pattern of atopic dermatitis in North Indian pediatric population. Pediatr Dermatol. 1998; 15:347–51.

6. Dhar S, Mandal B, Ghosh A. Epidemiology and clinical pattern of atopic dermatitis in 100 children seen in city hospital. Indian J Dermatol. 2002; 47:202–4.

7. Nagaraja, Kanwar AJ, Dhar S, Singh S. Frequency and significance of minor clinical features in various age-related subgroups of atopic dermatitis in children. Pediatr Dermatol 1996; 13: 10-3.

8. Böhme M, Svensson A, Kull I, Wahlgren CF. Hanifin's and Rajka's minor criteria for atopic dermatitis: Which do 2-year-olds exhibit? J Am Acad Dermatol 2000; 43: 785-92.

9. Mevorah B, Frenk E, Wietlisbach V, Carrel CF. Minor clinical features of atopic dermatitis. Evaluation of their diagnostic significance. Dermatologica 1988; 177: 360-4.

10. Kanwar AJ, Dhar S, Kaur S. Evaluation of minor clinical features of atopic dermatitis. Pediatr Dermatol 1991; 8: 114-6.

11. Parthasarathy N, Palit A, Inamadar AC, Adya KA. A study to estimate the frequency of Hanifin and Rajka's minor criteria in children for diagnosis of atopic dermatitis in a tertiary care centre in South India. Indian J Paediatr Dermatol 2019; 21: 31-5.

12. Agrawal DP, Lavanya MS, Sathyanarayana BD, Swaroop MR, Jain M, Dukkipati M. Evaluation of clinical diagnostic criteria of atopic dermatitis and serum IgE levels in patients with chronic eczema. Int J Health Sci Res 2015; 5: 84-9.

13. Li X, Yang H, Rabinowitz YS. Keratoconus: Classification scheme based on videokeratography and clinical signs. J Cataract Refract Surg 2009; 35: 1597-603.

14. Leung DY, Eichenfield LF, Boguniewicz M. Atopic dermatitis (Atopic eczema). In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's Dermatology in General Medicine. 8th ed. The McGraw-Hill Companies; 2012. p. 165-82.

15. Sarkar R, Kanwar AJ. Clinico-epidemiological profile and factors affecting severity of atopic dermatitis in North Indian children. Indian J Dermatol 2004; 49: 117-22.

16. Shetty NS, Lunge S, Sardesai VR, Dalal AB. A Cross-Sectional Study Comparing Application of Hanifin and Rajka Criteria in Indian Pediatric Atopic Dermatitis Patients to that of Other Countries. Indian Dermatol Online J 2022 Dec 29; 14(1): 32-37.

17. Kaujalgi R, Handa S, Jain A, Kanwar AJ. Ocular abnormalities in atopic dermatitis in Indian patients. Indian J Dermatol Venereol Leprol. 2009; 75: 148–51.