Review

Mycosis fungoides in pediatric population: comprehensive review on epidemiology, clinical presentation, and management

Rohit Kothari1, MD, Jacek C. Szepietowski2, MD, Martine Bagot3, MD, Sunmeet Sandhu4, MD, Anant Patil5, MD, Stephan Grabbe6, MD and Mohamad Goldust6, MD

1Department of Dermatology, Armed Forces Medical College, Pune, India, 2Department of Dermatology, Venereology and Allergology, Wroclaw Medical University, Wroclaw, Poland, 3Faculté de Médecine Paris Diderot, AP-HP, Service de Dermatologie, Hôpital Saint-Louis, Paris, France, 4Department of Dermatology, Command Hospital Air Force, Bangalore, India, 5Department of Pharmacology, Dr. DY Patil Medical College, Navi Mumbai, India, 6Department of Dermatology, University Medical Center of the Johannes Gutenberg University, Mainz, Germany

Correspondence
Mohamad Goldust, MD
Department of Dermatology
University Medical Center of the Johannes Gutenberg University
Mainz
Germany
E-mail: mgoldust@uni-mainz.de

Conflict of interest: None.

Funding source: None.

doi: 10.1111/ijd.16098

Abstract
Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma. However, it is rare in pediatric population. Most of the cases of pediatric MF present with hypopigmented patches and/or various other forms, which may often mimic common childhood dermatoses, thereby causing a delay in the diagnosis. There are no established treatment guidelines for pediatric MF. As the progression of childhood MF is extremely rare and it has an indolent course, it is usually diagnosed at an early stage (IA, IB, IIA), and hence phototherapy with a response rate of >80% is a well-established effective treatment in children. However, as recurrences are frequently seen on stopping the therapies, a maintenance regimen and long-term follow-up is equally important. This article reviews the epidemiological factors, clinical presentations, diagnosis, and various treatment modalities used in pediatric MF. We analyzed and compared the data of almost 616 childhood MF cases from various studies undertaken from 1988 to 2021.

Introduction
Primary cutaneous lymphomas are a heterogenous group of non-Hodgkin extranodal lymphomas arising from either T- or B-lymphocytes. Cutaneous T-cell lymphomas (CTCL) are the most common, and the incidence increases with age with an average age of 50 years at diagnosis.1 However, they are rare in pediatric population. Mycosis fungoides (MF), the most frequent type of CTCL, accounts for 38.7–65% of all primary cutaneous lymphomas in children2,3 and comprises almost 18% of the total MF cases including the adults.4 Due to the rarity, heterogeneous presentation, lack of standardized treatment guidelines, and at times morphology similar to common benign childhood dermatoses, it is often diagnosed late in children. This review attempts to give an overview and update on various epidemiological factors, clinical presentations, diagnosis, and management of pediatric MF.

Epidemiology

Incidence
The incidence of MF varies widely with the geographic location and age group of the population. It has an estimated incidence of around six cases per million per year in Europe and the United States, which accounts for 4% of all non-Hodgkin lymphomas,5 and pediatric MF accounts for almost 4–5% of the total MF cases.5,7
Age
MF can affect any age group, but the average age at disease diagnosis is 50–60 years.9 Pediatric age group represents a rare subset with most of the cases having onset between 6–8 years of age,7,9 and diagnosed at a mean age of 9–11 years10 illustrating a delay in diagnosis of approximately 1–5 years for many patients, however, may at times be up to 14–24 years in rare cases.11,12 The delay in diagnosis of pediatric MF may be due to avoidance of skin biopsy in children in addition to resemblance of MF lesions to various benign dermatoses in childhood like pityriasis alba, eczema, psoriasis, and vitiligo.13 Hence, MF was aptly called the “great imitator” by Zackheim et al.14

Sex
Slight male preponderance is seen in childhood MF, however, many studies reported a ratio between males and females close to 1 : 115 as compared to 2 : 1 seen in adults.4,11,16,17 Only few studies showed an increased incidence in female children with one of them reporting a ratio as high as 1 : 9 (M : F).18,19

Genetics
Several human leukocyte antigen (HLA) alleles have been associated with MF in adult population, namely HLA-DQB1 and HLA-DRB1, however, no statistically significant association was found between pediatric MF and any of these HLA alleles except HLA-B*73, the biological significance of which remains questionable due to its low frequency.20 Certain rare cases of familial MF have higher frequency of HLA-DQB1*03 as compared to controls (66.7% vs. 33%, respectively), which may support an association of this allele with the familial form of MF.21

Associated diseases
Pediatric MF has been reported in few cases to be associated with pityriasis lichenoides, atopic dermatitis, lymphomatoid papulosis, Wiskott-Aldrich syndrome, follicular mucinosis, and other malignancies.22–28

Clinical presentation
The classical presentation of MF in adults is gradually progressive asymptomatic scaly erythematous patches and plaques usually in the sun protected areas, which may progress to nodules/tumors over a period of several years.29 MF is typically characterized by a course in three stages: erythema/patch, plaque, and tumor stage. As children mainly show early forms of MF, patch stage is primarily observed. Most of the studies report hypopigmented MF as the predominant variant accounting for almost 55–100% of the cases.11,15,20,30–33 Other common variants reported are the classical MF, which may account for 15–40% of the cases,4,9,10,34,35 folliculotropic variant (3–36%),4,9,11,34 and poikilodermatous MF (5–26%).16,36

There are few uncommon variants which have been reported in children including pityriasis lichenoides chronica-like (PLC) MF, unilesional MF, pigmented purpuric dermatosis-like MF, granulomatous MF, ichthyosiform MF, hyperpigmented and intraoral presentation, inflammatory linear verrucous epidermal nevus-like MF, and pagetoid reticulosis, which may at times be difficult to diagnose at the initial presentation.20,37–44 Few rare cases of familial MF and MF post organ transplant have also been reported21,45,46 (Table 1). Mycosis fungoides with large-cell transformation in children is extremely rare and hence lacks a standardized therapeutic regimen. It is defined when the lymphoid infiltrate has more than 25% large cells with nuclei more than four times the normal size. It may present with erythematous patches, plaques, tumors, or nodules and has an aggressive course.47,48

Hypopigmented MF in childhood
The hypopigmented variant of MF in childhood is overrepresented and involves usually the trunk and extremities with lesions predominantly located on the sun protected sites. However, any site may be involved, and pruritus is a variable feature.49 It may be diagnosed late as it resembles many benign dermatoses in childhood like pityriasis alba, atopic dermatitis, tinea versicolor, post-inflammatory hypopigmentation, or other conditions like vitiligo, leprosy, sarcoidosis, hypopigmented parapsoriasis en plaque, and progressive macular hypomelanosis.50 Among Fitzpatrick skin type IV to VI, hypopigmented MF is more commonly seen in children, and it usually presents at a younger age as compared to children with other variants of MF.8,30,51

Stage
The majority of childhood MF cases are diagnosed at an early stage (IA, IB, IIA)4,15,31,34 while advanced disease like stage IIB and beyond is rare and carries a poor prognosis11,30 as they may end up reaching after a significant delay to the dermatologist or may be treated initially with some other close differential diagnosis as reported in one of the studies by Dulmage et al.

Table 1 Various forms of mycosis fungoides seen in pediatric population

| Common | Uncommon |
|--------|----------|
| 1. Hypopigmented MF (55–100%) | 1. Pityriasis lichenoides-like MF |
| 2. Classical MF (15–40%) | 2. Unilesional MF |
| 3. Folliculotropic MF (3–36%) | 3. PPD-like (pigmented purpuric dermatosis) MF |
| 4. Poikilodermatous MF (5–26%) | 4. Granulomatous MF |
| | 5. Ichthyosiform MF |
| | 6. Hyperpigmented MF |
| | 7. Intraoral MF |
| | 8. MF with large cell transformation |
| | 9. MF post organ transplant |

MF, mycosis fungoides.
wherein a tumor stage of childhood MF was initially managed with incision & drainage.\textsuperscript{52}

**Management**

**Diagnosis**

In children, poor response to treatment with the persistence of hypopigmented, papulosquamous, and purpuric lesions should raise a suspicion with MF as a differential diagnosis.\textsuperscript{30} The diagnosis of MF in children is thus based on the correlation of clinical, pathological, and, if necessary, additional tests such as radiology, flow cytometry, and molecular biological methods are useful. Invasive measures such as skin biopsy in case of children due to small age cause diagnostic difficulty and hence require a high degree of suspicion. Skin biopsy alone should not be used for the diagnosis of MF.\textsuperscript{4,6}

**Histopathology**

Most cases of pediatric MF have epidermotropism, atypical lymphocytes (82–100%), and haloed lymphoid cells in the epidermis and intraepidermal lymphocytes that are larger than dermal lymphocytes.\textsuperscript{3,10,19,31} Pautrier’s microabscess may be seen in 16–60% of the cases.\textsuperscript{10,13,31,49} Other features seen on histopathology include perivascular and periadnexal infiltrate, patchy lichenoid infiltrate, and psoriasiform epidermal hyperplasia. Epidermal atrophy is usually not seen (except in poikilodermatous MF).\textsuperscript{53} (Table 2).

**Histopathology in hypopigmented MF**

Along with epidermotropism, it shows minimal dermal involvement or fibroplasia of the reticular dermis.\textsuperscript{53,54} Also, unlike classic MF, which has a predominantly CD4\textsuperscript{+} phenotype, hypopigmented MF often displays a CD8\textsuperscript{+} T-suppressor phenotype. Hypopigmentation may be considered a good prognostic marker.\textsuperscript{55}

**Immunohistochemistry**

Epidermotropic peripheral T lymphocytes with phenotypes CD2\textsuperscript{+}, CD3\textsuperscript{+}, CD4\textsuperscript{+}, and CD5\textsuperscript{+} are the characteristic findings of MF tumor cells. The most consistent finding on immunohistochemistry is loss or reduced number of CD7\textsuperscript{+} lymphocytes, which may be seen in 70–90% of the cases even in early phases of the disease.\textsuperscript{9,13,19,53} Predominance of CD4\textsuperscript{+} T lymphocytes may be seen in 50–70% of cases\textsuperscript{11,13,36,53} while CD8\textsuperscript{+} T lymphocytes are seen in 20–67% of cases, more commonly in the hypopigmented variant (up to 100%).\textsuperscript{3,11,13,36,49,53} An overrepresentation of cytotoxic phenotype in children compared to adults has been previously observed in previous studies.\textsuperscript{42,56}

**Clonal T-cell receptor gene rearrangements**

Clonal T-cell receptor gene rearrangements are common in cases of adult MF patients, however, the data in pediatric cases is ambiguous with some studies showing no or lesser clonality ranging from 17–21%,\textsuperscript{7,13,48} while others showed a higher percentage of T cell clonality in almost 70–83% of cases.\textsuperscript{11,16,36}

**Treatment**

The treatment of childhood MF differs from that of adult cases in the form that almost all cases are diagnosed at an early stage (stage IA, IB, IIA) and they have less propensity to progress;\textsuperscript{5} hence, more amenable to treatment by skin directed therapies which include phototherapy which is the commonest modality used\textsuperscript{15} and topical corticosteroids (TCS), bexarotene, nitrogen mustard, vitamin D analogues, carmustine, pimecrolimus. Less commonly used therapies include interferon alpha (IFN), radiation therapy, acitretin and excimer laser, and extracorporeal photophoresis (ECP). ECP is used as a second line or rescue therapy in treatment-refractory MF.\textsuperscript{57} The studies on excimer 308 nm therapy in childhood MF are scarce and require further research, however, it may be beneficial in limited distribution cases.\textsuperscript{58}

Juvenile-onset MF generally has a comparably good prognosis and responds well to treatment; however, due to the potential long-term therapy in children, the treatments need to be chosen with care.\textsuperscript{15} Recurrences are frequently seen on discontinuing therapies, which signifies the importance of maintenance therapy and a long-term follow up.\textsuperscript{4,6} Treatment strategies for pediatric MF needs to be tailored on a case-by-case basis, and multiple factors should govern the choice of therapy including the age, stage, variant of MF, expectations of patient and the family and various adverse events associated with the therapy. Life expectancy in stage IA or IB disease of childhood MF has not shown any significant difference from that of general population, hence any intervention must have a favorable safety profile.\textsuperscript{19}

**Phototherapy**

Phototherapy treatment options include broadband UVB (BBUVB), narrowband UVB (NBUVB) (311 nm), psoralen with
### Table 3: Various studies (sample size ≥3) and the response to common treatment modalities

| Study                        | Total cases | Age Presentation | Stage | Therapy | Response |
|------------------------------|-------------|------------------|-------|---------|----------|
| **Ocampo OV et al. (2020)**  | 23          | 4-18 years; mean: 11 years; (10 F, 13 M) | Classic MF (26.1%), hypopigmented (52.2%), folliculotropic (17.4%), classic MF with capillaritis (4.3%) | IA (26.1%); IB (73.9) | Phototherapy: 22 1. PUVA: 14 (PUVA bath: 4, PUVA+IFN: 1) 2. NBUVB: 8 (with chemotherapy: 1) 3. TCS alone: 1 |
| **Kalay et al. (2020)**      | 4 (n = 29; four cases were children <20 years) | 6-19 years; mean: 13 years (2 F, 2 M) | Erythematous/hyperpigmented (25%), erythematous/hypopigmented (25%), hypopigmented (25%), hypopigmented with follicular hyperkeratosis (25%) | IA (50%); IB (25%), IIA (25%) | 1. TCS, topical bexarotene NBUVB: 1 2. Topical bexarotene gel: 1 3. PUVA with TCS: 1 4. PUVA with IFN: 1 |
| **Nasimi M et al. (2019)**  | 30          | 2-17 years; mean: 11 years (13 F, 17 M) | Hypopigmented (56.6%), patchy (20%) PPD-like (13.3%), PLC-like (3.3%), hypopigmented (3.3%), tumoral (3.3%) | IA and IB (96.6%); IIB (3.3%) | All treated with NBUVB 1. NBUVB: 2 (87%) 2. PUVA: 1 (33%) |
| **Amorim GM et al.**         | 3 (n = 20; 3 were children) | 10-17 years; mean: 12.6 years (3 M) | Hypopigmented in all (100%) | IA (67%); IB (33%) | 1. NBUVB: 2 (67%) 2. PUVA: 1 (33%) |
| **Virmari P et al. (2017)**  | 23 (n = 74 with age <30 years; 23 were children <20 years) | 6-20 years; Median: 17 years (11F, 12 M) | Hypopigmented (65.2%), classic (26%), folliculotropic (8.7%) | IA (30.4); IB (61%), IIB (61%) | 1. All early stage cases were treated with NBUVB, PUVA, UVA1 2. Topical agents (mid- & high-potent TCS, topical nitrogen mustard (bexarotene) 3. PUVA-IFN: 1 4. NBUVB-IFN: 1 |
| **Cervini AB et al. (2017)** | 14          | 8-15 years; mean: 11.23 years (6 F, 8 M) | Hypopigmented (100%), concomitant/subsequent classical MF (42.8%) | IA (14.3%); IB (78.5%), IIB (78.5%) | 1. CHOP QT & EBT (stage IVa2 case): 1 (7.2%) 2. PUVA-IFN + NBUVB: 1 (7.2%) 3. PUVA + TCS: 1 (7.2%) |
| **Jang MS et al. (2016)**    | 3           | 8-17 years; mean: 13.3 years (2F, 1 M) | Ichthyosiform MF in all (100%) | IB (100%) | 1. PUVA: 1 2. PUVA: 1 3. PUVA, acitretin: 1 |
| **Alikhan et al. (2014)**    | 3           | 11-19 years; mean: 14.9 years (3 M) | Folliculotropic (100%) | IA (100%) | 1. NBUVB: 2 (67%) 2. Topical bexarotene gel: 2 (67%) 3. 3. Minocycline 100 mg BD: 1 (33%) 4. Excimer laser: 1 (33%) |

**Remark:**
- **Kothari et al.** Mycosis fungoides and pediatric population Review 1461

- All received mid-potent to potent TCS alongside phototherapy
- Chemotherapy used: methotrexate, cytarabine and vorinostat
- At except 1 (treated with topical bexarotene gel) had relapses during follow-up (3-7 years) period
- >80 sessions of NBUVB had more chance of a totally or partially clearance
- TCS was given to 1 case with NBUVB; ≥100 sessions given to all
- Those still undergoing treatment were excluded
- No new lesions thereafter Responded to treatment but lesions remained
- PR, 6 years later relapse, NBUVB → CR 2. PR: 1 3. PR: 1 4. NBUVB: CR 5. NBUVB: PR 6. No new lesions thereafter
- PR, 6 years later relapse, NBUVB → CR 2. PR: 1 3. PR: 1 4. NBUVB: CR 5. NBUVB: PR 6. No new lesions thereafter
| Study                     | Total cases | Age                  | Presentation                                      | Stage     | Therapy                                                                 | Response          | Remark                                                                 |
|--------------------------|-------------|----------------------|--------------------------------------------------|-----------|------------------------------------------------------------------------|-------------------|------------------------------------------------------------------------|
| Boulos et al. (2014)³¹   | 34          | 4–19 years; median: 14 years (16 F, 18 M) | Hypopigmented (53%), hyperpigmented (29%), folliculotropic (3%) | IA (41%), IB (66%), IIB (3%) | 1. Phototherapy: 21 (62%) → NBUVB: 14, PUVA: 5, natural sunlight alone: 2. Nitrogen mustard: 3 (9%) 3. Topical retinoids: 5 (15%) 4. IFN: 6 (18%) |                  | 4. Excimer laser: CR with intermittent flaring 1. Phototherapy: CR (24%), PR (57%); progression: 10% (IA+IB with natural sunlight alone Stable disease: 10% disease 2. Nitrogen mustard: PR (33%) when combined with phototherapy and 67% had no clinical response 3. Topical tazarotene: CR (60%) in combination with phototherapy and other agents, PR: 20%, no clinical response: 20% 4. IFN: CR (67%) when combined with phototherapy and other agents, no clinical response: 17%, rest lost to follow up All cases that responded to NBUVB were hypopigmented MF |
| Heng et al. (2014)³¹     | 46          | Age range not given; mean: 10.3 years (14 F, 32 M) | Hypopigmented (91%), PLC-like (2%), PPD-like (2%), classical MF (2%), solitary MF (2%) | IA (39%), IB (69%), IIA (2%) | 1. Phototherapy → NBUVB: 32 (47%); PUVA: 3 (7%); UVA1: 1 (2%) 2. TCS alone: 8 (17%) |                  | 1. Phototherapy→NBUVB: CR in 15 (50%) with mean of 29.5 session; PUVA: CR in 0%, PR in 3 (100%) 2. TCS: No follow-up data Two cases chose to be treated at other institutions; 22% (7 patients) relapsed with NBUVB after a mean duration of 14.9 months |
| Hodak et al. (2014)⁹     | 50          | 0.75–18 years; mean: 7.4 (20 F, 30 M) | Hypopigmented (58%), FMF (26%), psoriasiform (20%), classical MF (16%), hyperpigmented (2%), unilesional (6%) | IA (52%), IB (6%), IIA (2%) | 1. Phototherapy → BB-UVB: 3 (8%); NBUVB: 13 (28%); PUVA: 9 (18%) 2. Topical nitrogen mustard: 2 (4%) 3. Surgical excision: 1 (2%) 4. Climatotherapy: 2 (4%) |                  | 1. Phototherapy for non-FMF disease: CR in 10 (71%) with BB-UVB & NBUVB; for FMF disease: CR in 7 (70%) 2. Topical nitrogen mustard: CR in 1 (50%) in combination with PUVA 3. Surgical excision: no follow-up 4. Climatotherapy: PR in 1 (50%); other was lost to follow-up |
| Koh MJ et al. (2014)³²    | 9           | 5–12 y; Mean = 8.8 y (1 F, 8 M) | Hypopigmented (100%) with concomitant pityriasis lichenoides (56%) | IA (22%), IB (67%), IIA (11%) | NBUVB: 9 (100%) |                  | CR in 8 (89%) by 9 months (3 of the 8 had sustained remission, 5 relapsed after 13 months Mean number of sessions: 57; 2-3 session/week were given with no difference in response for 2 week versus 3 week treatments 58% and 50% cases treated with NBUVB and PUVA respectively, required further course of phototherapy after 4 and 45.5 months respectively |
| Laws et al. (2014)³³      | 28          | Age range not given; mean: 11.6 years (15 F, 13 M) | Hypopigmented (79%), classic MF (21%) | IA (36%), IB (61%), not known (4%) | 1. NBUVB: 18 (64%) 2. Bath PUVA: 8 (29%) |                  | CR or PR in 86% (collectively for both NBUVB and PUVA) |
| Castano et al. (2013)³³   | 35          | 4–20 (20 M, 15 F) | Hypopigmented (100%) | Not reported | 1. Phototherapy→NBUVB: 19 (54%); PUVA: 1 (2%) 2. TCS alone: 6 (17%) |                  | 1. Phototherapy: PR in 16 (84%) and recurrence: 7 (20%) after discontinuation of therapy |

Table 3 Continued
| Study                          | Total cases | Age          | Presentation                        | Stage          | Therapy                          | Response                  | Remark                                      |
|-------------------------------|-------------|--------------|-------------------------------------|----------------|----------------------------------|---------------------------|---------------------------------------------|
| Yazganoglu et al. (2013)      | 20          | 2-18 years; mean: 9.20 years (8F, 12 M) | Hypopigmented (45%), unilesional MF (20%) | IA (45%), IB (15%), IIA (15%), IIB (20%) | 1. Phototherapy➔NBUVB: 6 (30%); PUVA: 3 (15%) | 2. TCS: CR in 2 (33%), PR in 2 (33%), no response in 2 (33%) | 3. Radiation: not recorded |
| Alsuwaidan et al. (2012)      | 5           | 6-13 years; mean: 9 years (5 M) | Hypopigmented (80%), classical MF (20%) | IA (80%), IIA (20%) | TCS or NBUVB | All had complete or almost complete response | Data on specific number of patients receiving NBUVB/TCS not given |
| Kim et al. (2009)             | 23          | 4-19 years; mean: 11 years (5 F, 18 M) | Hypopigmented (21%), PLC like (17%), classical MF (35%), other (30%) | IA or IB (100%) | 1. Phototherapy➔PUVA: 14 (61%); NBUVB: 3 (13%); UVA1: 4 (17%); Retinoic acid: 5 (22%); Calcipotriol: 4 (17%); Topical keratolytic: 2 (9%) | 1. Phototherapy➔PUVA: CR in 2 (14%) and PR in 12 (66%); NBUVB: CR in 3 (100%); UVA1: CR in 1 (25%) and PR in 2 (75%); Retinoic acid: PR in 5 (100%); Calcipotriol: PR in 4 (100%); Topical keratolytic: PR in 2 (100%) | 2. TCS: no recurrence in 4 (17%); No response in 1 (11%) and 1 (11%) patient was receiving therapy at time of study; Bexarotene: recurrence; Carmustine: Recurrence |

CR, complete response; MF, mycosis fungoides; PLC, pityriasis lichenoides chronica; PR, partial response.
UVA (PUVA) and UVA1. NBUVB is commonly used as first-line approach. Phototherapy has an affect on abnormal lymphocytes in MF.59 There is ample evidence on efficacy of PUVA and NBUVB in the treatment of pediatric MF with a response rate usually >80%. Both these modalities offer favorable outcome; PUVA therapy is penetrating deeper into the dermis compared to UVB therapy. However, the duration of remission may be greater with PUVA (30–87 months) as compared to NBUVB (4–29 months).19 NBUVB is preferred over PUVA in children due to the adverse effects of systemic psoralen, which may include risk of cataract or secondary skin cancers, while no such events are associated with NBUVB.19,60,61 The common side effects of both the therapies include erythema, blistering, lentigines, and irritation of varied degree. Oral psoralen should be avoided in children <10 years of age, and hence topical PUVA is a good alternative.62

The total number of treatment sessions can have a significant impact on the overall outcome, and a greater number of sessions (induction as well as maintenance) may be associated with prolonged remission and less relapses.30 Literature review over a period of 16 years (2005–2020) revealed 17 studies on childhood MF with sample size of ≥3 which revealed an overall response rate (complete and partial resolution) of 91% with PUVA and 70% with NBUVB4,6,10,30,41,63,64 (Table 3). The studies which did not report the specific number of cases who received either NBUVB or PUVA were not included.26,34

Topical therapy
It forms an integral part as an adjuvant or in few cases as the sole agent in the management of childhood MF. TCS are the most commonly used agents. TCS used alone in very early disease gave an average overall response of almost 50%.4,6 Recent studies involving topical bexarotene used as monotherapy in one patient and along with NBUVB and TCS in other achieved complete remission.63 Topical nitrogen mustard used in MF in 203 adults and children achieved an overall response rate of 83%.65 The rest of the topical agents are almost always used in conjunction with other therapies.

Systemic therapies
Certain rare presentations of pediatric MF like advanced stage, granulomatous MF, or cases of large cell transformation may need a more aggressive approach with total skin electron beam radiation therapy, methotrexate, oral bexarotene, interferon, liposomal doxorubicine, brentuximab vedotin, ifosfamide, etoposide, gemcitabine, polychemotherapy, and may require allogeneic hematopoietic cell transplant with a myeloablative regimen for a better outcome.10,48

Many newer agents like mogamulizumab, alemtuzumab, immune checkpoint inhibitors, histone deacetylase inhibitors (vorinostat, romidepsin, panobinostat, belinostat, and resminostat), pralatrexate, forodesine, denileukin diftitox, duvelisib, lenalidomide, and everolimus may be available, however, these are usually reserved for trials, advanced and refractory cases, and data for use in pediatric MF is lacking. They may form a part of future therapies in pediatric cases once sufficient data is available for each of these agents.66

**Prognosis**
In general, the prognosis of MF is stage dependent as the extent of skin involvement and presence or absence of extracutaneous disease are the main prognostic factors for the course of the disease. The overall prognosis in pediatric MF is good. Progression to advanced-stage MF during childhood seldom occurs (~3.3%).5 Survival rates at 5 and 10 years follow-up are 95% and 93%, respectively. The hypopigmented and poikilodermatous variant appears to have a better prognosis. CD8+ T cell immunophenotype is also associated with a better prognosis compared to adult-onset MF.36,63,64

**Conclusion**
Mycosis fungoides in the pediatric population is an uncommon disease. Diagnosis, and hence treatment, is usually delayed as it may mimic various common childhood dermatoses. As the majority of the patients has an early-stage disease (IA, IB, IIA) and favorable prognosis, phototherapy as first-line treatment is an effective treatment option for pediatric MF. Juvenile MF patients respond well to conventional therapy. Long-term follow-up and safety considerations of long-term treatment are needed in children. Due to a lack of standard treatment guidelines, there is a need to perform large scale studies to formulate effective and various patient tailored treatment regimens for the management of pediatric MF.

**Acknowledgments**
Open Access funding enabled and organized by Projekt DEAL.

**References**
1. Vaidya T, Badri T. Mycosis fungoides. [Updated 2020 Aug 26]. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519572/

2. Fink-Puches R, Chott A, Ardigo M, et al. The spectrum of cutaneous lymphomas in patients less than 20 years of age. *Pediatr Dermatol* 2004; 21: 525–553.

3. Ceppi F, Pope E, Ngan B, et al. Primary cutaneous lymphomas in children and adolescents. *Pediatr Blood Cancer* 2016; 63: 1886–1894.

4. Ocampo OV, Julio L, Zapata V, et al. Mycosis fungoides in children and adolescents: a series of 23 cases. *Actas Dermosifiliograficas* (English Ed.). 2020; 111: 149–156.

5. Amorim GM, Niemeyer-Corbellini JP, Quintella DC, et al. Clinical and epidemiological profile of patients with early stage mycosis fungoides. *An Bras Dermatol* 2018; 93: 546–552.

6. Wu JH, Cohen BA, Sweren RJ. Mycosis fungoides in pediatric patients: clinical features, diagnostic challenges, and advances in therapeutic management. *Pediatr Dermatol* 2020; 37: 18–28.
7. Yazganoglu KD, Topkarci Z, Buyukbabani N, et al. Childhood mycosis fungoides: a report of 20 cases from Turkey. J Eur Acad Dermatol 2013; 27: 295–300.

8. Ferenci K, Makkar HS. Cutaneous lymphoma: kids are not just little people. Clin Dermatol 2016; 34: 749–759.

9. Hodak E, Amitai-Laish I, Feinmesser M, et al. Juvenile mycosis fungoides: cutaneous T-cell lymphoma with frequent follicular involvement. J Am Acad Dermatol 2014; 70: 993–1001.

10. Cervini AB, Torres-Huamani AN, Sanchez-La-Rosa C, et al. Mycosis fungoides: experience in a pediatric hospital. Actas Dermofisiolgraficas (English Ed) 2017; 108: 564–570.

11. Boulos S, Vaid R, Aladily TN, et al. Clinical presentation, immunopathology, and treatment of juvenile-onset mycosis fungoides: a case series of 34 patients. J Am Acad Dermatol 2014; 71: 1117–1126.

12. Rodney IJ, Kindred C, Angra K, et al. Hypopigmented mycosis fungoides: a retrospective clinico-histopathologic study. J Eur Acad Dermatol Venereol 2017; 31: 808–814.

13. Ben-Amotz D, David M, Feinmesser M, et al. Juvenile mycosis fungoides diagnosed before 18 years of age. Acta Derm-Venereol 2003; 83: 451–456.

14. Zackheim HS, McCallmont TH. Mycosis fungoides: the great imitator. J Am Acad Dermatol 2002; 47: 914–918.

15. Jung JM, Lim DJ, Won CH, et al. Mycosis fungoides in children and adolescents: a systematic review. JAMA Dermatol 2021; 157: 431–438.

16. Nanda A, AlSaleh QA, Al-Ajmi H, et al. Mycosis fungoides in Arab children and adolescents: a report of 36 patients from Kuwait. Pediatr Dermatol 2010; 27: 607–613.

17. Nanda A, Al-Ajmi H. Mycosis fungoides in children and adolescents. Expert Rev Dermatol 2013; 8: 309–320.

18. Brazzelli V, Bernaccia C, Segal A, et al. Photophotochemotherapy in juvenile-onset mycosis fungoides: a retrospective study on 9 patients. Pediatr Hematol Oncol J 2019; 41: 34–37.

19. Laws PM, Shear NH, Pope E. Childhood mycosis fungoides: experience of 28 patients and response to phototherapy. Pediatr Dermatol 2014; 31: 459–464.

20. Reiter O, Amitai DB, Amitai-Laish I, et al. Pediatric mycosis fungoides: a study of the human leukocyte antigen system among Israeli Jewish patients. Arch Dermatol Res 2017; 309: 851–856.

21. Hodak E, Klein T, Gabay B, et al. Familial mycosis fungoides: report of 6 kindreds and a study of the HLA system. J Am Acad Dermatol 2005; 52: 393–402.

22. Borra T, Custin A, Saggini A, et al. Pityriasis lichenoides, atypical pityriasis lichenoides, and related conditions. Am J Surg Pathol 2018; 42: 1101–1112.

23. Onsun N, Kural Y, Su O, et al. Hypopigmented mycosis fungoides associated with atopy in two children. Pediatr Dermatol 2006; 23: 493–496.

24. Huang CH, Hsu CK, Lee JY. Lymphomatoid papulosis in association with mycosis fungoides: a clinical and histopathologic review of five Taiwanese cases. Dermatol Sin 2014; 32: 75–81.

25. Criscuolo M, Fiani L, Chiusolo P, et al. Allogeneic transplant for mycosis fungoides in patient with Wiskott-Aldrich Syndrome. J Clin Immunol 2018; 38: 7–9.

26. Alikhan A, Griffin J, Nguyen N, et al. Pediatric follicular mucinosis: presentation, histopathology, molecular genetics, treatment, and outcomes over an 11-year period at the Mayo Clinic. Pediatr Dermatol 2013; 30: 192–198.

27. Huang KP, Weinstein MA, Clarke CA, et al. Second lymphomas and other malignant neoplasms in patients with mycosis fungoides and Sézary syndrome: evidence from population-based and clinical cohorts. Arch Dermatol 2007; 143: 45–50.

28. Young GJ, Luu M, Izadi N. Mycosis fungoides in 2 pediatric patients with atopic dermatitis. J Allerg Clin Immunol In Practice 2021; 9: 2068–9.

29. Fatima S, Siddiqui S, Tariq MU, et al. Mycosis fungoides: a clinicopathological study of 60 cases from a tertiary care center. Indian J Dermatol 2020; 65: 123–129.

30. Nazmi M, Kamyab K, Aghahi T, et al. Childhood mycosis fungoides: a clinicopathologic study of 30 cases from Iran. Aust J Dermatol 2020; 61: e259–e261.

31. Heng YK, Koh MJ, Giam YC, et al. Pediatric mycosis fungoides in Singapore: a series of 46 children. Pediatr Dermatol 2014; 31: 477–482.

32. Koh MA, Chong WS. Narrow-band ultraviolet B phototherapy for mycosis fungoides in children. Clin Exp Dermatol 2014; 39: 474–479.

33. Alsouwaian SN. Childhood mycosis fungoides: new observations from the Middle East. J Saudi Soc Dermatol Dermatol Surg 2012; 16: 5–8.

34. Virmani P, Levin L, Myskowski PL, et al. Clinical outcome and prognosis of young patients with mycosis fungoides. Pediatr Dermatol 2017; 34: 547–553.

35. Kim ST, Sim HJ, Jeon YS, et al. Clinicopathological features and T-cell receptor gene rearrangement findings of mycosis fungoides in patients younger than age 20 years. J Dermatol 2009; 36: 392–402.

36. Wain EM, Orchard GE, Whittaker SJ, et al. Outcome in 34 patients with juvenile-onset mycosis fungoides: a clinical, immunophenotypic, and molecular study. Cancer 2003; 98: 2282–2290.

37. Amin SN, Muhamad R, Abdullah WN, et al. Pityriasis lichenoides-like mycosis fungoides in children: a challenging diagnosis. J Korean Acad Fam Med 2020; 42: 334–338.

38. Hodak E, Phenig E, Amichai B, et al. Unileisional mycosis fungoides. Dermatolog 2000; 201: 300–306.

39. Hanna S, Walsh N, D’Intino Y, et al. Mycosis fungoides presenting as pigmented purpuric dermatitis. Pediatr Dermatol 2006; 23: 350–354.

40. Wieser I, Wohlmuth C, Ducic M. Granulomatous mycosis fungoides in an adolescent—a rare encounter and review of the literature. Pediatr Dermatol 2016; 33: e296–e298.

41. Jang MS, Kang DY, Park JB, et al. Clinicopathological manifestations of ichthyosiform mycosis fungoides. Acta Derm-Venereol 2016; 96: 100–101.

42. Wain EM, Setterfield J, Judge MR, et al. Mycosis fungoides involving the oral mucosa in a child. Clin Exp Dermatol 2003; 28: 499–501.

43. Jang JG, Sim HJ, Kim SH, et al. Mycosis fungoides mimicking inflammatory linear verrucous epidermal nevus. J Eur Acad Dermatol 2004; 18: 218–220.

44. Miedler JD, Kristjansson AK, Gould J, et al. Pagetoid reticulosis in a 5-year-old boy. J Am Acad Dermatol 2008; 58: 679–681.

45. Vassallo C, Brazzelli V, Cestone E, et al. Mycosis fungoides in childhood: description and study of two siblings. Acta Derm-Venereol 2007; 87: 529–532.

46. Amin A, Burkhardt C, Groben P, et al. Primary cutaneous T-cell lymphoma following organ transplantation in a 16-year-old boy. Pediatr Dermatol 2009; 26: 112–113.
47 Chan WH, Lewis DJ, Hinojosa T, et al. Juvenile mycosis fungoides with large-cell transformation: successful treatment with psoralen with ultraviolet A light, interferon-alpha, and localized radiation. Pediatr Dermatol 2018; 35: e13–e16.
48 Gross AM, Turner J, Kirkorian AY, et al. A pediatric case of transformed mycosis fungoides in a BRCA2 positive patient. J Pediatr Hematol Oncol 2020; 42: e361–e364.
49 Pope E, Weitzman S, Ngan B, et al. Mycosis fungoides in the pediatric population: report from an international Childhood Registry of Cutaneous Lymphoma. J Cutan Med Surg 2010; 14: 1–6.
50 El-Darouti MA, Fawzy MM, Hegazy RA, et al. Hypopigmented parapsoriasis en plaque, a new, overlooked member of the parapsoriasis family: a report of 34 patients and a 7-year experience. J Am Acad Dermatol 2012; 67: 1182–1188.
51 Shabrawi-Caelen L, Cerroni L, Medeiros LJ, et al. Hypopigmented mycosis fungoides: frequent expression of a CD8+ T-cell phenotype. Am J Surg Pathol 2002; 26: 450–457.
52 Castano E, Glick S, Wolgast L, et al. Hypopigmented mycosis fungoides in childhood and adolescence: a long-term retrospective study. J Cutan Pathol 2013; 40: 924–934.
53 Gameiro A, Gouveia M, Tellechea Ó, et al. Childhood hypopigmented mycosis fungoides: a commonly delayed diagnosis. Clin Case Rep 2014; 2014: bcr2014208306.
54 Furlan FC, Sanches JA. Hypopigmented mycosis fungoides: a review of its clinical features and pathophysiology. An Bras Dermatol 2013; 88: 954–960.
55 Rustin MH, Griffiths M, Ridley CM. The immunopathology of hypopigmented mycosis fungoides. Clin Exp Dermatol 1986; 11: 332–339.