

Recommendations for Management of Childhood Psoriasis

Abstract

Childhood psoriasis is recognized as a potential multisystem disorder and hence it is imperative to optimize disease management to arrest progression, minimize psychological burden and evolution of metabolic syndrome. Clinical practice recommendations are necessary to assist practitioners in appropriate decision making based on available evidence. Owing to the lack of Indian recommendations on childhood psoriasis, the SIG Pediatric Dermatology under IADVL Academy undertook an evidence-based approach based on published literature on the topic, between January 2000 and July 2020 to frame the recommendations.

Keywords: *Childhood psoriasis, co-morbidity, phototherapy, recommendations, systemic, topical.*

Introduction

Psoriasis, an inflammatory immune mediated chronic multisystem disorder, constitutes 0.3-1.4% of all dermatoses presenting to a dermatological outpatient setting.^[1,2] The prevalence ranges from 0.1% to 11.8% worldwide and 0.44 to 2.8% in India, with peak age at onset in the third and fourth decades.^[3] Disease onset in the first two decades of life occurs in 20-35% of cases.^[4,5] Age of onset of childhood psoriasis ranges between 6.9-9.1 years resulting in significant morbidity in affected children.^[2,3] Epidemiological data on childhood psoriasis from India is however limited. In India, the prevalence of childhood psoriasis is 4.4%, constituting 3% of dermatology consultations and 12.5% of psoriasis cases.^[6,7] Childhood psoriasis, a well-recognized entity differs significantly from adult psoriasis with regards to clinico-epidemiological characteristics as well as the disease outcome.

Clinical practice guidelines comprising of systematically developed statements help both the physician as well as the patients in decision making with regards to treatment of specific clinical conditions.^[8] Research has shown that these guidelines being fundamental resources for providing optimal health care quality can improve the processes and outcome of care.^[9,10] Recently, guidelines for

the management of childhood psoriasis has been published by Joint American Academy of Dermatology and National Psoriasis Foundation.^[11] However, there is a need for recommendations specific to Indian setting owing to limited resources for management of childhood psoriasis. Hence, we as a special interest group (SIG) in pediatric dermatology under IADVL academy, present the recommendations.

Materials and Methods

The SIG pediatric dermatology comprising of seven members with special interest in pediatric psoriasis (at least more than five years of experience of managing pediatric psoriasis in high volume centres across various parts of the country) convened a meeting to identify relevant clinical questions regarding childhood psoriasis. An evidence-based approach was proposed and a literature search, encompassing studies, guidelines and recommendations published in English language between January 2000 and July 2020, was conducted in PubMed, MEDLINE and Cochrane Library databases. All studies including case reports, case series, observational studies, clinical trials, narrative and systematic review on childhood psoriasis were included. A total of 342 articles were screened using the search terms, out of which 98 articles were used to frame the recommendations.

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The medical subject headings (MeSH) terms and the various combinations used for literature search included the following: psoriasis, children, childhood, pediatric, guidelines, recommendations, diagnosis, severity, PASI, monitoring, comorbidities, psoriatic arthritis, metabolic syndrome, cardiovascular disorders, psychiatric disorders, nonalcoholic fatty liver disease, uveitis, inflammatory bowel disease, topical [emollients, coal tar, salicylic acid, anthralin, corticosteroids, steroids, calcineurin inhibitors (tacrolimus, pimecrolimus), vitamin D analogues (calcipotriol, calcipotriene, calcitriol), vitamin A, [tazarotene], phototherapy (BB-UVB, NB-UVB, targeted phototherapy, PUVA, Goeckerman therapy), ultraviolet therapy, psoralen, systemic (Methotrexate, Retinoids, Acitretin, Cyclosporine), biologicals (Adalimumab, Etanercept, Infliximab, Secukinumab, Ustekinumab, Ixekizumab), Apremilast, and complementary alternative medicine.

An iterative process was followed by the entire SIG group to review and edit the preliminary recommendations. Due to the ongoing pandemic situation, the members of the SIG group had 6 virtual meetings to frame the recommendations. During the initial meeting the relevant questions to be answered, literature search and search strategies were decided upon. The subsequent meeting had discussions with two experts. Based on their inputs, each member of the group was allotted specific topics who worked on literature search and drafted the preliminary recommendations which was shared with the group members. In the subsequent meetings, the recommendations were formulated and refined by the SIG members from interactive discussions based on literature researched and clinical experience. Independent views of each member on the practical application of the recommendations in Indian scenario was given which was then discussed and final consensus was reached. Levels of evidence and grades of recommendations were adapted as per the Oxford Centre for Evidence-Based Medicine Levels of Evidence (CEBM) [Boxes 1 and 2].^[12] Throughout the process of development of these recommendations, the conflicts of interests were disclosed by the SIG members and were reviewed for potentially relevant conflicts of interest.

Results and Discussion

Diagnosis of psoriasis in children

Clinical presentation of childhood psoriasis: The clinical presentation of childhood psoriasis is varied, and the diagnosis is most often clinical. Auspitz sign, Koebner's phenomenon and Woronoff ring can aid in clinical diagnosis. Though the clinical features of psoriasis in children are similar to that in adults, certain features are characteristic. In comparison to adults, the psoriatic plaques in children are thinner, softer, and less scaly, often affecting uncommon regions like the face, including

Box 1: Levels of evidence adapted from Oxford Centre for CEBM

- I-Systematic reviews of RCT or specific RCT
 - II-Systematic reviews of cohort studies or specific cohort study
 - III-Systematic reviews of case-control studies or specific case-control study
 - IV-Case-series or poor-quality cohort and case-control studies
 - V-Expert opinion
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Box 2: Grade of Recommendation adapted from Oxford Centre for CEBM

- A=Level I studies
 - B=Level II or III studies or extrapolations from level I studies
 - C=Level IV studies or extrapolations from level II or III studies
 - D=Level V evidence or inconsistent or inconclusive studies at any level
-

periorbital, perioral, and nasal regions and flexures. Chronic plaque psoriasis, observed in around 60% cases is the most common morphological type similar to adult disease. However, distinctive features in childhood include follicular involvement predominantly involving limbs and prominent pruritus present in 80% of the cases.^[13] The scalp is most frequently involved in childhood psoriasis, followed by extensor surfaces of extremities, trunk, nails, face, and ear.^[14] Involvement of hands, feet, genitals, and flexural areas, including the periumbilical area, is also common among children. Common differential diagnoses include eczema, tinea corporis and pityriasis rosea.

Napkin psoriasis, guttate psoriasis and palmoplantar psoriasis are commonly observed in children often with specific characteristics. Napkin psoriasis is the commonest manifestation seen in around 45% of cases of children aged less than two years.^[15] The presence of well-defined erythematous plaques with involvement of folds, presence of psoriasis in other sites including scalp, umbilicus, ear canal, periauricular region and perianal region, and family history of psoriasis helps to differentiate this from other causes of diaper dermatitis.^[16] Palmoplantar psoriasis occurring in association with chronic plaque psoriasis is more common than isolated palmoplantar involvement.^[6] Guttate psoriasis is more common among children than adults and seen in around 28% of them. It presents as small monomorphic round or ovoid papules and plaques ranging from 2-3 mm to 1 cm in diameter.^[17] About 60%, especially those with a younger age of onset and associated streptococcal infection, have resolution of the lesions within few months followed by long duration of remission. In the remaining 40%, guttate psoriasis tends to progress to the chronic plaque variant, particularly in those with a positive family history of psoriasis and without streptococcal infection.^[17] Common differentials of guttate psoriasis are pityriasis lichenoides and lichen planus.

Pustular psoriasis is very rare in children constituting around 1% of childhood psoriasis cases. It can affect infants as early as one month of age. Although data is insufficient, annular pustular psoriasis is considered to be the most common morphological type.^[18,19] Psoriatic erythroderma in children is very rare.

Nail involvement is observed in around 40% of the children with psoriasis, with pitting being the most common feature. Nail involvement is more common in males, severe psoriasis palmoplantar psoriasis, and psoriatic arthritis.^[20,21]

Psoriatic arthritis is rare in childhood, affecting 2-10% of children with psoriasis with an age at onset between 9-12 years. Small joints of hands and feet are commonly involved. The childhood arthritis and rheumatology research alliance (CARRA) registry for juvenile psoriatic arthritis reports a male predominance with high incidence of enthesitis.^[22]

Comparison of the clinical features of childhood psoriasis with adult psoriasis is provided in Table 1.

Risk factors for childhood psoriasis: The risk factors for development of childhood psoriasis include infections, stress, high body mass index [BMI], second hand tobacco exposure at home and drugs.^[27] Upper respiratory, vulval, perianal or perineal streptococcal infection and streptococcal balanoposthitis are associated with guttate psoriasis. Recent pharyngeal infection is associated with a seven-fold increase in the odds of developing guttate psoriasis.^[28] Withdrawal of oral or topical steroids and antimalarials are the more likely triggers among drugs in children than lithium and beta blockers seen in adults.^[4]

Family history of psoriasis is present in 23% of the cases.^[2,28] HLA-Cw6 is the commonest allele associated with familial psoriasis (55% in childhood onset psoriasis, 66% in familial cases) and these patients have early age of

onset, persistent guttate lesions, extensive plaques on limbs and trunk, severe disease, evidence of Koebnerization, worsening after throat infections, less incidence of nail and joint disease and better response to phototherapy.^[2,24] In children with very early onset of disease, severe refractory disease and suggestive clinical patterns, DIRA (deficiency of IL-1 receptor antagonist), DITRA (deficiency of IL-36 receptor antagonist) and CAPE (CARD-14 associated papulosquamous eruption) should be considered in the differentials. DIRA and DITRA present with a generalized pustular psoriasis morphology while CAPE presents commonly with treatment resistant patterned plaques, erythroderma, pustular lesions or arthritis.^[29] Such monogenic forms of psoriasis need to be considered in severe childhood onset psoriasis which is refractory to conventional treatment.

Diagnostic tools in childhood psoriasis: Psoriasis in children is diagnosed clinically and there are no validated clinical diagnostic criteria yet. Histopathological features of psoriasis include parakeratosis, hypogranulosis, elongated rete ridges, Munro's micro abscess (neutrophils in stratum corneum), suprapapillary thinning, dilated dermal blood vessels and perivascular lymphocytic infiltrate.^[13] Hyperkeratosis and parakeratosis of nail bed and hyponychium are the most common biopsy findings in nail psoriasis in adults and a diagnosis could be made in 67% by histopathology. However, there is not much information available on histopathology of nail psoriasis in children.^[30]

Regularly arranged red dots with mild background erythema and white scales are the most predictive dermoscopic features of plaque psoriasis.^[31] These features can be used to differentiate psoriasis from pityriasis rosea and lichen planus and also help to differentiate scalp psoriasis from seborrheic dermatitis.^[32]

Table 1: Clinical Features of Childhood Psoriasis Versus Adult Psoriasis^[23-26]

Features	Childhood psoriasis	Adult psoriasis
Type of lesions	Plaque type most common Guttate psoriasis and follicular psoriasis are commonly seen Napkin psoriasis in infants Severe forms like erythroderma and pustular psoriasis are rare	Plaque type is most common More extensive and severe disease
Features of psoriatic plaques	Thinner, softer and less scaly plaques Pruritus more common	Thicker plaques with white scales Pruritus less common
Patient characteristics	Female preponderance Family history more common HLA Cw6 positivity	Male preponderance Lesser prevalence of family history and HLA Cw6 positivity
Location of lesions	Though elbows, knees, scalp and lower back are the common sites, facial and scalp lesions are more common than adults	Extensor of extremities
Triggers	Infections, stress and trauma are common triggers Drugs are uncommon	Drugs are more common triggers than in childhood type
Prognosis	Better than adults More chances of complete remission	Waxing waning course Less chance of spontaneous remission

Reflectance confocal microscopy shows parakeratosis, tortuous dermal vessels and Munro's micro abscess. Munro's micro abscess has a sensitivity of 90% and specificity of 96% in stable psoriasis vulgaris.^[33] However, this tool is not easily available or widely used.

Cutaneous high frequency ultrasound has been used to measure the epidermal hyperplasia (measured as the epidermal thickness) and dermal infiltration and edema (measured as dermal thickness) and can be used as a quantitative tool to assess progression in plaque psoriasis.^[34] It can be used to assess the improvement with treatment by doing serial measurements before and during treatment.^[35] Nail ultrasound including power doppler and spectral doppler ultrasound can measure the thickness of ventral and dorsal nail plates, nail bed, loss of definition, morphological changes and blood flow disturbances.^[36]

Criteria based on diagnostic models (genetic and molecular), histopathology, skin imaging, and questionnaires have been identified in a systematic review on the diagnostic criteria for psoriasis in adults and children. Dermoscopic criteria for psoriasis has a sensitivity of 45-98% and specificity of 88-99%. Video-dermoscopy scalp psoriasis severity index had poor inter-observer reproducibility. Weighted genetic risk scores based on 10 known psoriasis susceptibility genes helps to capture the risk of familial psoriasis.^[33] However the practical use of these scores are limited as they are useful only in familial cases, expensive and are not easily available.

Coexistence of nail psoriasis and onychomycosis can be seen in 46-47% cases of nail psoriasis. Nail psoriasis makes the nail plate easily penetrable to fungal elements and presence of onychomycosis can worsen nail psoriasis by Koebnerization, making prompt diagnosis and management essential.^[37] In pediatric population, onychomycosis is rarer than in adults and may be restricted to 1 digit. KOH examination may be necessary especially in patients with only toe nail involvement, those with features of onycholysis and subungual hyperkeratosis or those with diffuse single nail plate crumbling.^[20]

International League of Associations for Rheumatology (ILAR) criteria is used for the diagnosis of childhood psoriatic arthritis in a child with arthritis and psoriasis or arthritis with two of the following: dactylitis, nail pitting or first degree relative with psoriasis, and absence of rheumatoid factor positivity.^[38] X-ray in a child with psoriatic arthritis tends to show non-specific findings like osteopenia and soft tissue edema than the classical features of psoriatic arthritis like acro-osteolysis, periosteal new bone formation, and periostitis. Early erosions in children may not be seen as the joints still have a lot of cartilaginous component.^[39] Ultrasonography can be a useful and relatively inexpensive tool to pick up changes in case of clinically silent synovitis and can be used for early diagnosis.^[40]

USG can also detect joint effusion with 90% sensitivity in clinically active joints and 70% sensitivity in clinically inactive joints.^[41] Contrast enhanced MRI is useful in detecting early changes of psoriatic arthritis especially of the synovium, joint spaces and bone marrow where X-ray is normal or atypical. The most common changes observed are diffuse, contrast enhancing synovial thickening, followed by joint space effusion (mostly small) and diffuse enhancement of bone marrow in both non articular and articular sites (suggestive of bone marrow edema). Other soft tissue changes like periarticular atrophy and tendon changes like thickening, edema, tendon sheath fluid or enhancement (most commonly on hands) could also be picked up on MRI.^[42] Though MRI is a sensitive modality of detecting pediatric psoriatic arthritis, it is lengthy, needs contrast enhancement, sedation in children and is limited to one joint or area at a time. Hence its use is restricted to doubtful cases where it would play a role in decision making or in complex involvement especially of the sacroiliac joint and temporo mandibular joint.^[39]

Practice points: The diagnosis of pediatric psoriasis should be made on clinical grounds. Biopsy and dermoscopy may be used to aid in diagnosis. ILAR criteria should be used to diagnose psoriatic arthritis in children. Evidence of streptococcal infection in guttate psoriasis may help in prognosis. HLA-Cw6 status can help to predict the clinical course and long-term prognosis. X-ray is the standard modality of diagnosis of psoriatic arthritis. Ultrasound can be used in suspected cases and can pick up synovitis and joint effusion.

Level of evidence: II, III

Strength of recommendation: C, D

Assessment of severity and monitoring of childhood plaque psoriasis

To assess the severity of plaque psoriasis, psoriasis area severity index (PASI) and body surface area (BSA) are the commonest tools used. Rule of 9 can be used to assess BSA in children with psoriasis. Based on BSA, disease can be divided into mild (<3%), moderate (3-10%) or severe psoriasis (>10%).^[43] PASI (0-72) takes into account erythema, induration and scaling along with area of involvement. But available literature on the practicality of using PASI score in children is limited. Along with the physical distress due to disease, a major impact of psoriasis is on the psyche and needs to be taken into account to assess the severity of disease.^[44] Quality of life in childhood psoriasis is impaired similar to adult-onset psoriasis with specific impact on the social development domain.^[43] Childhood dermatology life quality index (CDLQI) is a simple yet validated questionnaire with 10 questions which can be used to assess psychosocial impact of psoriasis in children.^[45] A cartoon version with pictures is available for easier use in children.^[46] Quality of life is also known to

change with change in PASI.^[47] Other scales like physician global assessment and simplified psoriasis index have also been used in children.^[27] A value of BSA >10, PASI >10 or DLQI >10 is considered as severe psoriasis for most clinical trials. Recently, there has been a recategorization of severity of psoriasis as mild psoriasis in cases managed by topical therapy alone and moderate to severe psoriasis in cases that require systemic therapy (phototherapy, nonbiologic systemic therapy and biologics), BSA >10% and disease involving special areas (scalp, face, nails, palms, soles, genitalia) and failure of topical therapy.^[48] Even in children with BSA and PASI <10, a high CDLQI might warrant systemic therapy.

Practice point: BSA is a simple tool to measure severity of pediatric psoriasis. PASI can be used when feasible. CDLQI should be measured in all children with psoriasis.

Level of evidence: III

Strength of recommendation: C

Screening for co-morbidity in childhood psoriasis

Pediatric psoriasis is now understood to affect multiple organ systems similar to that observed in adults. The co-morbidities associated with pediatric psoriasis include obesity, dyslipidemia, diabetes mellitus, hypertension, nonalcoholic fatty liver disease (NAFLD), inflammatory bowel disease, arthritis, uveitis, polycystic ovarian syndrome (PCOS), mood disorders, substance abuse and poor quality of life in general.^[49] Uveitis is more common in children with psoriatic arthritis (8-18%).^[22]

BMI more than 85-95% is overweight while BMI more than 95% is obese. Increased cytokines secondary to excess adipose tissue leads to psoriasis. Adiposity, waist circumference and waist hip ratio are high in children with psoriasis with a three-fold increased incidence of obesity among them. There is good quality evidence for the association of overweight and obesity with childhood psoriasis.^[49,50] Since adults with psoriasis have increased dyslipidemia and the risk of myocardial infarction is high among young adults with severe disease, early preventive strategies are important.^[51] Among the various criteria used to diagnose metabolic syndrome in children, International Diabetes Federation (IDF) criteria for 6-16 year old is commonly used.^[52] An independent risk of dyslipidemia, diabetes mellitus, NAFLD, PCOS and elevated liver enzymes in children with psoriasis irrespective of obesity status was observed in a large retrospective study while Badaoui *et al.*, in their systematic review reported a true association of pediatric psoriasis with overweight and obesity only.^[53,54]

Children with psoriasis were observed to have an increased risk of acquiring anxiety, depression, and bipolar disorder compared to controls with the increased risk being highest for anxiety (HR = 1.32) followed by

depression (HR = 1.25).^[55] Patient health questionnaire 4 [PHQ4] can be used for anxiety and depression screening in children.^[56]

However, data on co-morbidities in Indian children with psoriasis is limited. Among Indian children with psoriasis, Vitamin D deficiency, obesity and metabolic syndrome were reported in 77.4%, 10.7% and 14.5% cases, respectively.^[2]

Pediatric psoriasis co-morbidity screening guidelines (2017) and the American Academy of Dermatology-National Psoriasis Foundation (AAD-NPF) guidelines are clear on the need for comorbidity screening at various points during the disease course.^[11,49] Major emphasis has been made on the point of educating the patient and care giver regarding these comorbidities and on appropriate liaison with the concerned specialties in case a comorbidity is detected.

The key guidelines include:

- a. Yearly screening of obesity and overweight by BMI charting is recommended from 2 years of age.
- b. Three yearly screening for diabetes mellitus by fasting blood glucose levels from 10 years of age in overweight children who have 2 of the following risk factors: family history of type 2 diabetes in first- or second-degree members, certain ethnicities, gestational diabetes or maternal diabetes in pregnancy.
- c. Three yearly screening for diabetes mellitus by fasting blood glucose levels in obese children starting from puberty, irrespective of other risk factors.
- d. Screening for dyslipidemia during 2 age ranges: 9-11 years and 17-21 years by measuring total cholesterol, LDL, HDL and triglycerides. Additional measurements to be done in children with cardiovascular risk factors. Those with dyslipidemia or metabolic syndrome should be referred to an endocrinologist/physician for management.
- e. Screening for hypertension by measuring blood pressure yearly from 3 years of age and comparing to age, sex and height reference charts.
- f. Screening all obese children and those who are overweight with additional risk factors for NAFLD by measuring ALT (alanine amino transferase) starting from 9-11 years of age (repeat 2-3 yearly if normal). Earlier screening in children with severe obesity, family history of NAFLD or hypopituitarism.
- g. Screening for arthritis by clinical examination at the time of diagnosis as well as periodically, based on symptoms. Patients with arthritis should be referred to a rheumatologist at the earliest.
- h. Yearly screening for depression and anxiety irrespective of age and appropriate referral.
- i. Yearly screening for substance abuse starting from 11 years of age and appropriate referral.
- j. Screening for other diseases like inflammatory bowel disease, polycystic ovaries and uveitis when clinically warranted. Uveitis screening should be done in

all children with psoriatic arthritis and others with symptoms by an ophthalmologist.

These recommendations can be extrapolated to the Indian scenario till there are further studies on Indian children with psoriasis regarding comorbidities and preventive strategies.

Practice points: We recommend screening at diagnosis and/or at appropriate age ranges for obesity, type 2 diabetes mellitus, hypertension, dyslipidemia, NAFLD, anxiety, depression and arthritis in all children with psoriasis. We also recommend that patients and care givers should be educated about these risks so that appropriate mitigation strategies can be undertaken by them.

Strength of evidence: II, III

Level of recommendation: C

Treatment of childhood psoriasis

(1) Topical therapy

The first line therapy of psoriasis in childhood and adolescence is use of topical agents. They are the main stay of therapy for mild or localized disease with PASI <10 or BSA <10%.^[57] Despite their extensive use in children, all topical agents are still used as off label indications for psoriasis owing to the lack of studies in pediatric population.

(a) Topical corticosteroids:

Though topical steroids have been extensively used in the management of psoriasis owing to their anti-inflammatory, immunosuppressant, and antiproliferative properties, clinical trials on the use of topical steroids in psoriasis in the pediatric population is lacking. Topical steroids are widely used for localized disease both for the control of flares as well as for maintenance therapy.^[11] The agents of choice are class 2 and 3 topical corticosteroids. High potent steroids like clobetasol propionate (0.05%) and Halobetasol (0.05%) have been found to be efficacious with minimal side effects when used for a limited duration of 1-2 weeks and avoiding their use on face, genitalia and flexures. Maintenance therapy can be done using mid to low potent steroid. High-potent corticosteroids should be used for brief duration or in combination with steroid-sparing agents (in children >3 years) owing to the larger body surface area in children, which poses the risk of potential systemic absorption and adrenal suppression. In very sensitive areas (face, axillae, genitalia) also, topical steroids (\leq class 2) should be used only for shorter duration (1-2 weeks). On the scalp, class 4 corticosteroids can be used for initial treatment. Sudden discontinuation may sometimes lead to clinical deterioration and rebound flares and hence corticosteroids should always be tapered and stopped. After 1-2 weeks of once-daily application, steroids can

be tapered to alternate day application till sustained clinical improvement is achieved after which they can be continued twice weekly for a few weeks.

Practice points: We recommend once daily use of class 2 and 3 topical steroids for mild to moderate localized plaque psoriasis, class 1 and 2 steroids for sensitive areas like face, axillae, genitalia and class 4 steroids for scalp, palms and soles for a limited duration of 1-2 weeks after which it needs to be gradually tapered and stopped. Topical steroids can also be used as part of rotational therapy.

Level of Evidence - II

Strength of Recommendation - B, C

(b) Topical calcineurin inhibitors:

Topical Tacrolimus (0.03 and 0.1%) and Pimecrolimus (1%) are used as off label indications in pediatric age group, as larger clinical trials and evidences are lacking in literature. Though they have been shown to be relatively less efficacious in psoriasis, they can be used for sensitive areas like intertriginous and facial psoriasis.^[58] They have been recommended as first line therapy for face, genitalia and flexures in a systematic review.^[59] The most common side effect reported is a burning or stinging sensation immediately after application. Apart from this, pruritus and irritation have also been reported.^[58,60] Studies on prolonged use of pimecrolimus have found no evidence of increased oncogenic risk in children whereas data regarding tacrolimus is inconsistent suggesting a minimal increase in the risk of lymphoma.^[61]

Practice points: We recommend the use of topical calcineurin inhibitors (Tacrolimus above 2 years of age and Pimecrolimus above 2 months of age) as first line therapy for psoriasis involving face, flexures and genitalia.

Level of Evidence: III

Strength of Recommendation: C

(c) Topical vitamin D analogues:

These include Calcipotriol (calcipotriene), Calcitriol and Tacalcitol. They are antiproliferative agents promoting keratinocyte differentiation. Vitamin D analogues can be started while tapering topical corticosteroids and need be continued after stopping corticosteroid therapy. Vitamin D analogues are considered safe in pediatric age group because of its steroid sparing effect but should be avoided for application in larger surface areas, due to risk of local irritation and of theoretical risk of systemic hypercalcemia due to transcutaneous absorption.^[62,63] Calcipotriene once daily application should be used on less than 30% of BSA and Tacalcitol on less than 15% of BSA. Use should also be avoided in sensitive area like face, flexures and genitalia,^[64] because of local irritation. Several studies have shown excellent outcomes with good tolerance in mild to moderate disease.^[65,66] However, vitamin D analogues are contraindicated in children below 2 years of age.^[67]

Practice points: We recommend vitamin D analogues, Calcipotriol and Calcitriol, in children above 2 years of age for the treatment of chronic plaque psoriasis and nail psoriasis. It should be avoided in lesions over face, genitalia and flexures. For children above 12 years of age, the total dose should not exceed 75 g/week while for those between 6 to 12 years of age, it should not exceed 50 g/week.

Level of Evidence - II, III

Strength of recommendation - B

(d) Other topical agents:

(i) Emollients: Emollients form an occlusive barrier and prevent the trans-epidermal water loss thereby maintaining the hydration of stratum corneum while natural moisturizing factors increase the water binding capacity. They alter the electrical properties of stratum corneum and in turn have an anti-inflammatory effect as well. Emollients also help in increasing the penetration of topical corticosteroids. White soft paraffin has shown to reduce the Koebner phenomenon in psoriasis. Experimental studies have shown that oil-in-water emollients when applied prior to phototherapy enhance the penetration of UVA or UVB. However, emollients such as petrolatum may have a blocking effect. Creams and ointments, which are thicker, are preferred over lotions. Patients with psoriasis should be advised to apply emollients liberally following warm water bath which needs to be reapplied for the second or third time throughout the day. Contact dermatitis (irritant and allergic), fragrance allergy and pigmentary changes are occasional side effects. In conclusion, emollients are an essential supportive modality which help in reducing the scaling and itching while improving the barrier function thereby resulting in better patient acceptance.^[68]

(i) Keratolytics: To enhance the penetration of topical therapeutic agents it is essential to remove the psoriatic scales, for which various keratolytic agents like lactic acid, dimethicone and salicylic acid have been commonly used. However, salicylic acid needs to be used with caution in children, owing to its life-threatening systemic toxicity. Salicylic acid is contraindicated in infants and children below two years of age owing to the risk of systemic absorption.^[69]

(ii) Anthralin: Anthralin (dithranol) can be used in pediatric psoriasis due to its very good safety profile as it does not have percutaneous absorption. Several studies have concluded its safety and efficacy in pediatric psoriasis.^[70,71] However, due to its skin-irritating properties, and staining of skin and clothes, its use is limited; especially in children.^[57]

(iii) Coal tar: Coal tar has anti-inflammatory, antipruritic and antiproliferative properties and hence used in the treatment of psoriasis. Irritation, staining, and unpleasant odor limits its use in children. Since benzene

has carcinogenic effects, longer duration of application of tar is not recommended in children.^[72]

(iv) Tazarotene: Tazarotene though approved in adult psoriasis, has not been approved in children as evidence for its use in childhood psoriasis is limited to a single case report.^[73] Irritation, pruritus and burning sensation are the common adverse effects but these can be reduced by combining with topical corticosteroids. It also reduces corticosteroid-induced atrophy. It can be considered for use in nail psoriasis and localized hyperkeratotic lesions.^[11]

(e) Topical Combination and Rotational therapy:

Combination therapy with topical agents in pediatric psoriasis has been advocated because of synergistic effect, improved therapeutic outcome and improved patient adherence. Combination therapy of Calcipotriol and Betamethasone dipropionate is FDA approved and several studies have established the safety and efficacy of this combination.^[74-76] Rotational therapy with topical corticosteroids, calcineurin inhibitors, vitamin D analogues, and emollients used in a tailored approach reduces steroid dependence, improves safety profile and decreases the risk of adverse effects of the individual topical agents when used in long term.^[77]

Practice points: We recommend the use of combination of vitamin D analogues and topical corticosteroids for their synergistic action and improved therapeutic outcome. Rotational therapy with various topical agents improves the safety profile.

Level of Evidence - II

Strength of recommendation - B, C

The various topical agents used in management of pediatric psoriasis is summarized in Table 2.

(II) Phototherapy:

Phototherapy has been commonly used in the treatment of psoriasis in combination with topical and systemic agents. Broad experience on the use of phototherapy in adult psoriasis exists along with the availability of adequate clinical studies and guidelines; however, its use in childhood psoriasis is limited. Early or prolonged use of phototherapy in children is associated with lot of challenges owing to the risk of retinal toxicity, accelerated or premature skin aging and induction of skin malignancy.^[78] However, despite the lack of randomized control trials (RCT) on the effect of phototherapy in childhood psoriasis, all studies conducted till date have demonstrated significant response to phototherapy with minimal adverse effects in children with psoriasis.^[79-81]

Phototherapy is well tolerated in children with psoriasis and is indicated in debilitating palmoplantar psoriasis, chronic plaque psoriasis involving 5-10% of BSA, refractory psoriasis or children in whom systemic drugs are contraindicated.^[82] Main modalities used

Table 2: Topical Agents Used in Pediatric Psoriasis

Drug	Dosage	Indication	Level of Evidence	Strength of Recommendation
Corticosteroids	0.05% Halobetasol cream; 0.05% clobetasol cream	Lower potency: face, genitalia and intertriginous areas High potency: hyperkeratotic areas, like palms and soles	II	B, C
Vitamin D analogues	Calcipotriene (calcipotriol)	Maximum dose that can be applied 6-12 years: 50 g/ week >12 years: 75 g/week	II	B, C
Calcineurin inhibitors	0.03% and 0.1% Tacrolimus ointment; 1% Pimecrolimus cream	Intertriginous and facial psoriasis lesions	III	C
Salicylic acid	6% ointment, 3% shampoo	Scalp psoriasis and palmoplantar psoriasis. Children aged 6 years or more.	-	-
Coal tar	0.5-20% Ointment, cream or solution	Mainly for plaque type lesions.	-	-
Anthralin (dithranol)	Concentrations up to 1%	“Short-contact” or “minute” therapy	-	-
Topical retinoids	Tazarotene 0.05%, 0.1%	Plaque psoriasis, nail psoriasis	-	-

are: broadband ultraviolet B (BB-UVB, 280–320 nm), narrowband (NB)-UVB (311–313 nm) and UVA (320–400 nm). They cause inhibition of DNA synthesis and keratinocyte proliferation, induce T lymphocyte apoptosis and produce anti-inflammatory mediators.

Oral psoralen plus UV-A (PUVA) otherwise known as photochemotherapy is best avoided in pediatric age group because of long term toxicity and insufficient data of its use in recent times. Topical PUVA therapy has been found to be effective in childhood psoriasis in few reports and has been recommended by few authors to be used in children above ten years of age when alternative options are not available. However, it is not often preferred owing to the lack of data on its long-term effects in children pertaining specifically to photo-carcinogenesis and reports of increased systemic absorption in cases with extensive disease and high PASI.

Guttate psoriasis responds excellently to BB-UVB. NB-UVB, being less erythemogenic than BB-UVB is now considered the first line phototherapy and is effective for guttate or thin plaque psoriasis.^[83] Dryness, erythema, pruritus, blistering and activation of herpes virus are short-term side effects of UVB while premature photoaging and carcinogenesis are the long-term side effects though not well documented in children.^[84] However patient's compliance and treatment adherence could be significant issues. Studies showing safety and efficacy of combination treatment with other systemic agents like oral retinoids, Methotrexate, Apremilast are lacking in pediatric age group. Nevertheless, in practice combining these modalities can have a positive outcome.

Recommendations to follow while using phototherapy:

- Proper patient selection with parent's consent, adequate counselling and patient education.
- Counselling is required regarding compliance and treatment adherence, requirement for long term treatment and importance of following precautions.

- Disruption of schooling for regular therapy needs to be taken into consideration.
- Children might face separation anxiety or feel anxious or claustrophobic while being in the chamber. This can be addressed by constantly engaging them in conversations during the treatment session or providing the child with toys to play with or keep the chamber open or allow parents fully dressed into the chamber for the initial few sessions until their anxiety subsides.
- In localised disease, home-based hand-held phototherapy devices may be used for paediatric patients after proper counselling of parents as these home-based devices are less frightening to children.
- Pre-treatment with emollients.
- Adequate eye protection with UVB protective goggles and genitalia protection with covered clothing.
- Erythrodermic psoriasis, photosensitive genetic disorders and cutaneous malignancies are absolute contraindication.
- Combination with other systemic or topical therapy should be advocated.

Dosage and Duration:

- The starting dose is 50-70% of the minimal erythema dose (MED) assessed for each patient.
- Increase in dose at each visit is 5-20% of the previous dose.
- Frequency of sittings should be thrice weekly at beginning and can be tapered to twice weekly in subsequent weeks based on clinical improvement.
- Significant response is usually seen in between 25-35 sittings.
- Very high cumulative doses are to be avoided.
- Cycles must be restricted to 2-3 per year.

Dose adjustment for missed treatment:

- Missed doses up to 1 week- previous doses to be maintained.
- Missed doses up to 2 weeks - reduce dose by 25%

- Missed doses up to 3 to 4 weeks- reduce dose by 50-75%.
- Missed doses more than 4 weeks- restart initial starting dose.

Practice points: We recommend narrow band UVB therapy as the most effective and safe phototherapy in pediatric age group. Guttate and severe plaque psoriasis shows the best response. More than 30-35 sittings at continuous stretch should be avoided and cycles must be restricted to 2-3 per year.

Level of Evidence: II, III

Strength of recommendation: B, C

(III) Systemic therapy in childhood psoriasis:

Systemic therapy for management of childhood psoriasis is decided based on baseline disease severity, disease activity, subtype, response to topical and phototherapy, associated physical or psychological impairment, and presence of comorbidities. In children with psoriasis, systemic therapy is used for the management of severe types of psoriasis including generalized plaque type unresponsive to topical therapy or phototherapy, pustular and erythrodermic forms.^[11,85]

The goal of therapy in children should focus on controlling or clearing the disease followed by maintenance of disease stability for several months after which the drugs can be tapered to the lowest effective dose and then transitioned off. Thus, the preferred approach would be long-term maintenance with the least toxic therapy with the lowest effective dose. Nevertheless, limited therapeutic preferences and poor compliance are major limitations in the management of childhood psoriasis.^[85] However, with considerable progress in the treatment of pediatric psoriasis, safe and efficacious therapeutic options in children are quite promising.

Systemic therapy of moderate to severe childhood psoriasis includes conventional non biologic therapies like methotrexate, acitretin, cyclosporine and biologic therapies like Etanercept, Adalimumab, Ustekinumab, Ixekizumab and Secukinumab which are currently licensed for use in children with moderate-to- severe plaque psoriasis.^[11,85] However, many of these treatments used in adults like Methotrexate, Cyclosporine and Infliximab are not approved by the FDA or EMA for use in children.

A. Methotrexate:

Literature on use of Methotrexate for treatment of psoriasis in children is limited and is mostly based on retrospective series and limited number of cases. One long term prospective study on methotrexate in pediatric psoriasis the Child-Capture registry reported that Methotrexate significantly improved PASI and quality of life scores with a good safety profile.^[74] In an Indian study on 24 children with severe psoriasis treated with Methotrexate, >75% reduction in PASI was observed in majority of cases and

PASI 50 was attained at 5 weeks. Methotrexate was well tolerated with mild side effects.^[86] Methotrexate has also been found to be useful in children with pustular psoriasis.

Thus, Methotrexate being a readily available, cheap, effective and relatively safe drug, it can be used for management of severe psoriasis in children as a first line systemic therapy with regular monitoring for side effects especially hepatotoxicity.^[3] However, liver fibrosis has not been reported in children with psoriasis on methotrexate and hence liver biopsy is not recommended.^[11] Since methotrexate has a slow onset of action ranging between 4-12 weeks with peak action at 3-4 months, it is used for management of chronic plaque psoriasis. It can be used as monotherapy as well as combination with phototherapy and as sequential therapy with cyclosporine for maintenance after control of acute flare of disease. Methotrexate has been recommended to be used for a duration of at least 24 weeks before discontinuing because of ineffectiveness.^[11,27,86]

Practice points: We recommend methotrexate as a first line effective systemic therapy for moderate to severe plaque psoriasis and pustular psoriasis in children at a dose of 0.3-0.5 mg/kg/week, to be continued till PASI 75 is achieved, and then to be tapered gradually.^[87] Folic acid should be supplemented at a dose of 1 mg/day, on 6 days of the week except on the day of methotrexate. Routine laboratory monitoring of blood counts, liver enzymes and creatinine needs to be done before and during treatment with methotrexate.

Level of evidence: II

Strength of recommendation: B

B. Acitretin:

Acitretin is considered the first line effective, non-immunosuppressive systemic therapy for childhood psoriasis which can be safely used in children of all ages as early as 6 weeks of life. Acitretin can be used for widespread guttate or moderate to severe thin plaque psoriasis, pustular psoriasis and palmoplantar psoriasis. It can be used in combination with phototherapy for synergistic effect requiring dose reduction in both therapies. Acitretin can be used as sequential therapy for disease maintenance following Cyclosporine. Response occurs after 2 to 3 months in chronic plaque psoriasis while it is immediate within 72 hours in pustular psoriasis. Most common clinical adverse effects observed with acitretin are mucocutaneous effects and transient and dose dependent hyperlipidemia and hepatotoxicity. Bony changes have not been reported even on long term therapy with doses of 1 mg/kg/day in children with psoriasis and hence there is no consensus yet on a monitoring protocol for bony changes in children on acitretin for psoriasis unlike in congenital ichthyosis.^[11,27,78,88]

Practice points: We recommend acitretin as a first line effective, non-immunosuppressive systemic therapy for

children with widespread guttate or moderate to severe thin plaque psoriasis, pustular psoriasis and palmoplantar psoriasis at a dose of 0.1 to 1 mg/kg/day.^[11] Acitretin in combination with NB-UVB therapy results in dosage reduction of both agents. Routine laboratory monitoring of liver enzymes and lipid profile needs to be done before and during treatment with acitretin.

Level of evidence: II

Strength of recommendation: B

C. Cyclosporine:

Cyclosporine has been reported to be an effective and well tolerated drug for management of psoriasis in childhood and adolescence in a multicentre retrospective study as well as in an Indian retrospective study.^[89] Response starts in 1-2 weeks with full effect occurring by 4-8 weeks. Hence, cyclosporine is used as a crisis drug for rapid disease control in severe forms of disease like unstable, erythrodermic and pustular psoriasis. Cyclosporine can be used in all ages and has been used for pustular psoriasis in infants as young as 10 months. However, children generally require a four times higher dose when compared to adults, owing to the altered pharmacokinetics of Cyclosporine in children associated with less absorption and faster clearance. Renal toxicity, dyselectrolyemia and hypertension are important side effects that need to be monitored for. cyclosporine needs to be gradually tapered and shifted to a safer alternative for long-term maintenance. It should never be combined with photo- or photochemotherapy due to risk of non-melanoma skin cancer.^[11,27,78]

Practice points: We recommend cyclosporine at a dose of 2 to 5 mg/kg/day in two divided doses as a short-term crisis drug (2-3 months) for management of severe or unstable plaque, erythrodermic, or pustular psoriasis. Cyclosporine is continued until PASI 75 is attained, after which Cyclosporine can be gradually tapered, and the child can be shifted to a safer alternative for long-term maintenance. Routine monitoring of blood pressure, laboratory monitoring of blood counts, serum electrolytes (potassium, magnesium), creatinine, lipid levels (cholesterol, triglycerides) need to be done before and during treatment with cyclosporine.

Level of evidence: III

Strength of recommendation: C

D. Biologics

Biologics in childhood psoriasis are recommended when first or second-line therapies fail to control disease in severe plaque psoriasis. Etanercept, Adalimumab, Ustekinumab, Secukinumab and Ixekizumab have been approved in childhood psoriasis. However, the evidence is limited only for moderate to severe plaque psoriasis and has been used as off label indications for other severe forms. Biologics can be safely combined with topical agents as well as with methotrexate to prevent resistance due to

antibody formation. However, the safety or efficacy data for the combination therapy is lacking in children. Three biologic agents (Etanercept, Adalimumab and Infliximab) have long term safety data with no major side effects when used up to one year. The issues that need to be considered while using biologics include long term safety, infections and vaccination. Live vaccines need to be given six months after stopping therapy and at least 1-3 months prior to starting therapy and household contacts need to be vaccinated prior to treatment initiation. Screening for viral infections (HIV, hepatitis) and annual screening for tuberculosis needs to be done and treatment needs to be withheld during major infections. Other investigations are not routinely recommended unless clinically indicated. There are no recommendations yet on safe transition between biologic and non-biologic therapy.^[11,27,78,90-93]

Practice points: We recommend biologics for management of extensive and severe psoriasis with significant psychosocial impact/functional impairment/involvement of high impact and difficult to treat sites or in situations wherein all or at least two traditional systemic therapies and/or NB-UVB phototherapy have failed, or not tolerated or contraindicated, or persistent psoriasis that relapses rapidly within 3 months of completion of treatment. Etanercept is recommended for moderate to severe plaque psoriasis in children ≥ 6 years as subcutaneous injection at a dose of 0.8 mg/kg/week to a maximum of 50 mg. Adalimumab is recommended for moderate to severe plaque psoriasis in children ≥ 4 years as subcutaneous injection at a dose of 0.8 mg/kg to a maximum of 40 mg at weeks 0 and 1 and thereafter every alternate week. Ustekinumab is recommended for moderate to severe plaque psoriasis in children ≥ 12 years at a dose of 0.75 mg/kg if < 60 kg, 45 mg if 60 to < 100 kg, and 90 mg if > 100 kg at 0, 4, and 16 weeks and then every 12 weeks. Secukinumab has been currently approved (August 2020) by the European Commission for moderate-to-severe plaque psoriasis in children and adolescents aged between six and 18 years at a dose of 75 mg for < 50 kg and 150 mg for those 50 kg or more which can be increased to 300 mg.^[94] It has also shown to be effective in nail psoriasis and psoriatic arthritis in a child.^[95] Ixekizumab has been FDA approved in March 2020 for children aged 6 years or older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy with weight based dosing as 160 mg at Week 0, followed by 80 mg every 4 weeks for > 50 kg, 80 mg at Week 0, followed by 40 mg every 4 weeks for 25-50 kg, 40 mg at week 0, followed by 20 mg every 4 weeks for < 25 kg.^[96] Infliximab is recommended for the management of rapidly progressive or unstable, and/or life-threatening pustular psoriasis that is unresponsive to other systemic medications either as monotherapy or in combination with Methotrexate.

Purified protein derivative test (PPD) or interferon-gamma release assay for latent tuberculosis should be done at

baseline and repeated annually with regular monitoring for infections during treatment.^[11]

Level of evidence: I, III (Infliximab)

Strength of recommendation: A (Etanercept), B (Adalimumab, Ustekinumab), C (Infliximab)

The various systemic agents used in management of pediatric psoriasis is summarized in Table 3.

E. Newer drugs in the horizon for childhood psoriasis:

Newer drugs like IL-17 inhibitors (Brodalumab) and IL-23 inhibitors (Guselkumab, Risankizumab) that have been effective in adults with moderate to severe chronic plaque psoriasis are being currently investigated in childhood psoriasis.^[90] Similarly, the phosphodiesterase 4 inhibitor, Apremilast which has been approved for the treatment of moderate to severe plaque psoriasis and active psoriatic arthritis in adults has been found to be effective in phase II trial for childhood psoriasis.^[97]

(IV) Complementary and alternative medicine:

Complementary and alternative medicine comprises of medical and healthcare systems, practices, and products outside the conventional medical practice. The use of these medicines is common among patients with psoriasis especially in India which is known for its traditional medicinal system. Recently, a protocol has been proposed for a Cochrane Review on complementary medicine as a treatment option for chronic plaque psoriasis which includes a subgroup analysis on children <18 years.^[98] However, there is no published literature yet on use of complementary and alternative medicine in childhood psoriasis.

An algorithm for the management of pediatric psoriasis is provided in flowchart 1.

Psychosocial support:

Psoriasis being a chronic disease with recurrent remissions and exacerbations, has a significant impact on the quality of life of the children especially during their adolescence, and their parents as well. Hence the entire family requires psychosocial support to help them overcome the psychological burden. The help of a psychologist or counsellor would be beneficial to these patients. The child and their family need to be counselled regarding the nature and course of the disease and they should learn to cope up with the disease. The importance of adequate management to arrest disease progression and prevent the development of disfiguring lesions and evolution to multisystem disease needs to be stressed upon. Realistic expectation of disease control rather than cure from treatment needs to be emphasized.

Long term follow-up

Pediatric psoriasis with an early age at disease onset puts the child at risk for long term complications of the disease as well as its treatment. The chronicity and recurrence of disease predisposes the child to cumulative toxicities of drugs. Moreover, long term safety data of the drugs used for psoriasis treatment are not available for children. Psoriasis being a multisystem disease thus requires a long term follow up and monitoring for associated co-morbidities as per recommendations, long term side effects of treatment and psychosocial impact of disease.

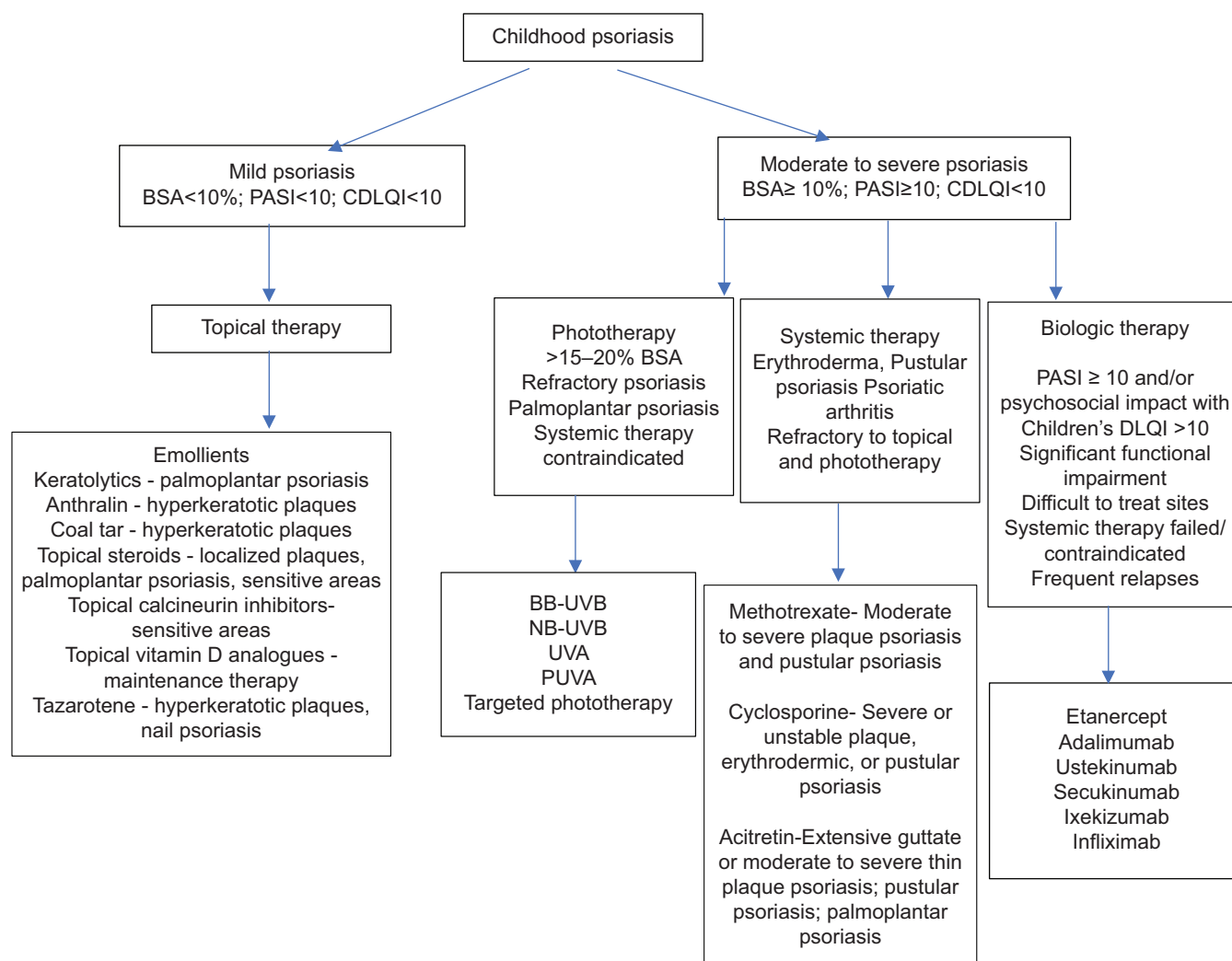
Conclusion

Pediatric psoriasis is thus a well-recognized entity which significantly differs from adult psoriasis with respect to

Table 3: Systemic Agents Used in Pediatric Psoriasis

Drug	Dosage	Indication	Level of Evidence	Strength of recommendation
Methotrexate	0.3-0.5 mg/kg/week, to be continued till PASI 75	Moderate to severe plaque psoriasis and pustular psoriasis	II	B
Acitretin	0.1-1 mg/kg/day	Widespread guttate or moderate to severe thin plaque psoriasis, pustular psoriasis and palmoplantar psoriasis	II	B
Cyclosporine	2-5 mg/kg/day in two divided doses	Severe or unstable plaque, erythrodermic, or pustular psoriasis	III	C
Biologics	Etanercept - 0.8 mg/kg/week to a maximum of 50 mg, subcutaneous injection. Adalimumab - 0.8 mg/kg to a maximum of 40 mg at weeks 0 and 1 and thereafter every alternate week, subcutaneous injection	Moderate to severe plaque psoriasis in children ≥ 6 years	I	A
		Moderate to severe plaque psoriasis in children ≥ 4 years	I	B
		Moderate to severe plaque psoriasis in children ≥ 12 years	I	B
	Ustekinumab - 0.75 mg/kg if <60 kg, 45 mg if 60 to <100 kg, and 90 mg if >100 kg at 0, 4, and 16 and then every 12 weeks.			

PASI: psoriasis area and severity index



Flowchart 1: Algorithm for the management of pediatric psoriasis

clinical presentation, management and outcome. The key goal of treatment is reduction in disease severity so as to improve the quality of life. However, long-duration treatment with phototherapy or drugs needs detailed evaluation owing to the chronicity and recurrences. Hence there is a need for national guidelines specific to pediatric population for timely diagnosis and adequate management with the available resources. Significant knowledge gaps exist with respect to childhood psoriasis and studies on the epidemiology as well as management of childhood psoriasis is limited from India and the current recommendation is framed based on worldwide recommendations which has been modified to be applied to our patients. Hence, there is a need for long term prospective studies on management of childhood psoriasis from India to generate adequate scientific evidence based on which national guidelines suitable to our population can be proposed.

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Conflicts of interest

There are no conflicts of interest.

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