

# Childhood psoriasis: A review of literature

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**Abstract** Psoriasis is a chronic inflammatory, immune-mediated disease in which one-third of patients suffer under the age of 18 years. In early age, the diagnosis may be difficult because of the atypical lesions. Plaque type of psoriasis is the commonest form of childhood psoriasis. Phototherapy as well as systemic therapy used in childhood psoriasis has limited use because of the long-term side effects of the drugs like teratogenicity, low tolerance, and other liver, renal and hematological derangements. In this review, the update on clinical aspects of childhood psoriasis, its onset, precipitating factors, demographics, pathogenesis and therapeutic options are discussed.

**Key words**

Psoriasis, childhood, systemic therapy, topical therapy.

## Introduction

Psoriasis vulgaris is a genetically-determined inflammatory dermatosis which affects around 3.5% of population in USA<sup>1</sup> whereas it occurs with a relatively less frequency in Pakistan (unpublished observations). It exhibits a bimodal age distribution i.e. one, childhood psoriasis that occurs before 18 years and, second, adult psoriasis that develops above 18 years. Childhood psoriasis is further categorized as: i) infantile psoriasis (onset within first year, a self-limited disease), ii) psoriasis with early onset, and iii) pediatric psoriasis with psoriatic arthritis.<sup>2</sup> Congenital psoriasis (psoriasis from birth), is associated with a lower prevalence of relevant family history, a different pattern of anatomic involvement, a higher fraction of erythrodermic, pustular or linear subtypes, and, having a poor prognosis. Hence, it is suggested that congenital psoriasis should be considered in erythematous, scaling, or

pustular eruptions in the newborn.<sup>3</sup> The aim of this article is to review the current literature of childhood psoriasis and update its clinical aspects, pathogenesis and treatment.

## Onset of the disease

The incidence of childhood psoriasis is unknown,<sup>4</sup> but it has been reported that 10% of all cases occurred before the age of 10 years and 2% at less than 2 years of age.<sup>5</sup> The differences of onset between females and males have varied from region to region.<sup>6</sup> In a study from India, the onset of the disease was noted from 4 days to 14 years. The mean age of onset was  $8.1 \pm 2.1$  years in boys and  $9.3 \pm 2.3$  years in girls. The peak age of onset in boys was in the 6-10 years age group, whereas the majority of the girls showed an onset of psoriasis between the ages of 10 and 14 years.<sup>7</sup> In another report which was carried out in 277 childhood psoriatic patients from China, it was found that the mean age of their patients was 11 years. The male:female ratio in their patients was 1:1.13. The median age of onset of disease in their patients was 10 years.<sup>8</sup> Furthermore, a population based study was performed to see the incidence cohort in patients less than 18 years in US. Authors

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observed that annual incidence of pediatric psoriasis was 40.8 per 100,000. They concluded that the incidence of pediatric psoriasis is increasing with increasing of age, and there is no specific peak in psoriasis, and both the males and females suffer equally.<sup>9</sup> In contrast, in a recent study, no evidence found index in childhood, disease severity in later life or type of treatments used.<sup>10</sup> In a retrospective study in under 18 years in 61 childhood psoriasis patients from Turkey, authors found that 23 (37.7%) were boys and 38 (62.3%) were girls, hence no specific difference was detected between the male and female ratio. The mean age of girls was  $9.28 \pm 4.02$  years and of boys  $11.18 \pm 3.85$  years. The mean age of onset of disease in girls was  $6.81 \pm 4.11$  years and in boys were  $7.03 \pm 4.28$  years. In 14 (23%) cases, a positive family history was detected.<sup>11</sup>

### **Precipitating factors**

The association of childhood obesity (overweight) and the psoriasis is considered among one of the prevalence factors. In Italy the prevalence of overweight in preschool children was estimated to be 4.4%<sup>12</sup> while in adolescents (age 10-16 years) it was 14.9%.<sup>13</sup> In a further study, which was conducted to observe the influence of obesity on childhood psoriasis, the positive findings were observed and it was concluded that being overweight is an important risk factor for the onset of childhood psoriasis.<sup>14</sup> It has been noted that childhood overweight is also associated with a variety of adverse consequences such as cardiovascular diseases, type 2 diabetes and sleep apnea. It is suggested that psoriasis should be added to the adverse consequences of childhood obesity.<sup>15</sup> In a study from Turkey, authors found that in most of their patients the triggering factors were respiratory tract infections (14.8%) and positive throat culture for group A  $\beta$ -hemolytic streptococci (21.3%). Also, the frequency of emotional stress and

psychiatric morbidity was 54% and 9.8%, respectively. It is suggested that stress and upper respiratory infections are the most important triggering factors in childhood and adult psoriasis.<sup>11</sup> The proposed trigger factors in generalized pustular psoriasis are medications, bacterial infections, sunburns, pregnancy, use of coal tar, emotional stress, vaccination, hypocalcaemia, and withdrawal of corticosteroids.<sup>16,17</sup>

### **Clinical presentation**

Most of the children manifest with plaque type psoriasis (68.6%) in similar pattern to adult patients, with lesions localized to the scalp, postauricular region, elbows, and knees. Guttate disease is more common in pediatric than adult patients, seen in 28.9% of 277 children in a Chinese survey. Other patterns in childhood psoriasis were erythroderma (1.4%), pustular disease including palmoplantar pustular psoriasis (1.1%), and mucosal glossitis (1.1%).<sup>8</sup> Another study has shown the most frequent clinical type of childhood psoriasis as a plaque type in 1302 (68.1%) of patients, followed by guttate psoriasis in 727 (38.0%) of patients. Erythrodermic psoriasis and pustular psoriasis were only seen in 7.3% and 5.0% of patients, respectively.<sup>10</sup> Though, in children, the generalized pustular psoriasis is uncommon but may present as a severe and potentially life-threatening disorder. Four clinical patterns of pustular psoriasis have been described in children: generalized pustular psoriasis, annular pustular psoriasis, exanthematic pustular psoriasis, and localized pustular psoriasis. They are not necessarily mutually exclusive and mixed variants are also possible. Generalized pustular psoriasis even in a 6 week old infant has been reported.<sup>18</sup> In case of congenital psoriasis, the erythrodermic psoriasis stands second after the plaque-type psoriasis, followed by the pustular psoriasis.<sup>19-22</sup> The most frequent localizations at onset have also been seen on trunk (44.3%),

extremities (54.0%), and scalp (36.0%).<sup>11</sup> In a congenital psoriatic patients, the observed affected areas in descending order were face, extremities, scalp, trunk, generalized distribution, buttocks, diaper area and palms and planter surfaces of feet.<sup>6,21,23</sup>

### **Pathogenesis**

The exact pathogenesis of psoriasis has not been completely discovered; however, it is agreed on that psoriasis has a genetic basis, as 23.4% to 71% of children will have a family history of psoriasis.<sup>6,11</sup> HLA-Cw6 has been known to be a susceptibility gene in psoriasis.<sup>24</sup> The guttate psoriasis subset may have been linked to inflammatory focus in about two-thirds of patients. Cross-reactivity of keratinocytes antigens with streptococcal antigens is thought to accelerate psoriatic lesions.<sup>25</sup> Among the other infections found in psoriatic disease are the presence of staphylococcal superantigens<sup>26</sup> and HPV DNA.<sup>27</sup> No single gene has been found to be responsible for psoriasis vulgaris. A series of genes have been observed having the mutation association with psoriatic disease, they are IL12-B9, IL 13, IL-23R, HLABW6, and so on. These genes play a role in Th2 cell and Th 17 cell activity as well as NF-kB signaling, demonstrating both a role for Th2 and Th17 lymphocytes in the pathogenesis of psoriatic disease. The pathogenesis of psoriasis is a result of the activation of several types of leukocytes that control cellular activity and T cell dependant inflammatory process in skin that accelerates the growth of epidermal and vascular cells in psoriasis lesions. The process can be broken down into three steps: initial activation of T cells in the lymph nodes draining the skin in response to an antigen, migration of effector T cells into the skin harboring the activating antigen, and the effector function of T cells in the skin.<sup>28,29</sup> The T cells in psoriasis lesions are mainly activated type 1 helper T cells (Th1) (CD4+) and type 1

cytotoxic T cells (suppressor) (Tc1) (CD8+). The activation of T lymphocytes could be due to bacterial antigens or others. The activated lymphocytes secrete cytokines which include interleukin-2 (IL2), tumor necrosis factor alpha (TNF- $\alpha$ ) and gamma interferon ( $\gamma$ -INF). These cytokines cause keratinocytes and endothelial cells stimulation which contribute to the hyperproliferation of epidermal cells in psoriasis.<sup>30,31,32</sup>

### **Treatment**

Psoriasis is a genetic disorder; although the exact cause of this disease is unknown but various factors are being considered having the role in pathogenesis. All types of adult psoriasis have been found in children with more or less frequency. Therefore, the similar treatment regimens have been tried in childhood psoriasis. The use of topical therapy in childhood is the firstline of treatment for skin limited disease, but with the chronicity of illness and in more severe cases, systemic therapy and phototherapy are added to help the remission. Well-designed studies on systemic therapeutic modalities for psoriasis in pediatric age group are meager and children are treated with the support of data extrapolated from that in adults.<sup>33</sup> Significant psychological disturbances are seen in children with psoriasis, irrespective of the involved surface area.<sup>34</sup> The opinion is that the chronic disease should be treated more aggressively to improve the quality of life because this may cause severe psychological disturbance.

#### ***Topical treatment***

There are various agents which are frequently used as topical therapies for childhood psoriasis. Topical steroids are usually prescribed similar to atopic dermatitis, mild type of corticosteroids for the face and moderate to potent type of steroids for the body and scalp. Long time usage of potent steroids may cause atrophy if wide area of

body surface is involved. Topical clobetasol has been recommended for the use in children ages 12 and over.<sup>35,36</sup> Anthralin 1% or dithranol are rarely used in childhood psoriasis because of causing local irritation.<sup>37</sup> Other topical preparations like calcipotriene or calcitriol can be used for childhood psoriasis. When topical calcipotriol was used in 2-14 years age in 43 psoriatic children, it was found significantly more effective than the vehicle control.<sup>38</sup> Among the other topical agents useful in childhood psoriasis are topical calcineurin inhibitors, tacrolimus 0.3% and pimecrolimus 1%.<sup>39</sup>

### **Phototherapy**

Phototherapy is considered safe and effective treatment for children who are able to follow the protocol of phototherapy. Generalized or hand-foot therapy, either narrowband ultraviolet-B (NB-UVB), UVB or psoralen and UVA (PUVA) can be used. In 12-week NB-UVB treatment, PASI 90 was achieved in 60% of patients, however, 10% had less than 50% improvement.<sup>39</sup> A series of 113 children were treated with various phototherapy procedures. It was observed that 92.9% of psoriatic patients treated by NB-UVB, 83.3% treated with PUVA and 93.3% treated with UVB showed positive response.<sup>40</sup> NB-UVB and PUVA therapies have also shown the satisfactory results in the treatment of childhood guttate and plaque psoriasis. Marked improvement was found in 88% of the 25 patients treated.<sup>41</sup> In 35 cases clearance of disease was found in 63% of cases.<sup>42</sup> Only few cases are reported to develop the erythema and anxiety during phototherapy, otherwise, it is being well tolerated.<sup>43</sup> Although, phototherapy is a simple and natural way of treatment but simultaneously both the children and parents must be educated for the hazards of overexposure.

### **Systemic treatment**

Systemic treatment is ultimate option which may be used in severe and uncontrolled psoriasis. Immunosuppressive drugs like methotrexate, acitretin or cyclosporin may be used for a time period of 6 months.

### **Oral antibiotics**

Oral antibiotics are useful in psoriasis particularly when the oral pharyngeal culture is positive.<sup>44,45</sup> However, the use of oral antibiotics has shown mixed results.<sup>46</sup> When the two patients received thiamphenicol (20 mg/kg/d), the lesions were found cleared less than 50%.<sup>47</sup> In a series of four patients treated with erythromycin (50mg/kg/d) for two weeks, the lesions disappeared completely.<sup>48</sup> In another report, a patient with guttate psoriasis was treated with amoxicillin/clavulanic acid (50 mg/kg/d) and all lesions cleared after 20 days of treatment.<sup>49</sup> Other antibiotics may be tried accordingly.

### **Cyclosporin**

Cyclosporin is an oral immunosuppressant drug which is basically used for the prevention of transplant rejection, and can be used in childhood psoriasis with the dose of 3 to 5 mg/kg body weight. Due to serious side effects the use of cyclosporine is limited and the patients need to be monitored regularly. Precautions are required to have repeated look on high blood pressure and renal function tests by conducting the serum urea nitrogen and creatinine tests. Malignancy and lymphoproliferative disorders are among the serious side effects of this drug but due to the limited and low dose usage these side effects might be decreased.<sup>50</sup> Three patients of pustular psoriasis were treated with cyclosporin in a dose of 1 to 2 mg/kg/d; two of them showed complete disappearance of lesions after 6 and 9 months, respectively, whereas the third patient showed significant improvement after five month treatment.<sup>51</sup> Another patient with pustular psoriasis was

treated with cyclosporine (3mg/kg/d), the authors observed the complete remission of disease after 11 months.<sup>52</sup> In contrast, in another study, none of four patients showed any response to this treatment.<sup>53</sup>

#### *Retinoids*

Retinoids are among the other treatment options being used in psoriasis. Due to severe side effects, this drug may not be selected as first-line therapy in childhood psoriasis. Because of the teratogenic effects, this drug should be used carefully in childbearing age females. Bony changes may occur after the long term treatment. There are other side effects like elevation in lipids and alteration in blood counts etc. Despite the severe long term side effects, acitretin orally 0.5 to 1 mg/kg per day has been used for disorders of cornification and psoriasis with good results.<sup>54</sup> In a retrospective review, etretinate was given in 10 cases with initial dose of 1mg/kg per day, with a duration varying from 3 weeks to more than 12 months. All patients with pustular psoriasis (n=5) achieved complete clearance of lesions; but, in contrast, erythrodermic psoriasis subgroup (n=5) showed the complete clearance of lesions in two patients only and the remaining three patients showed partial improvement.<sup>55</sup> Cheilitis, pruritus and hair loss were often observed during the use of retinoids. Skin fragility and focal osteoporosis were other side effects noted.<sup>55</sup> A 16-year-old girl with childhood generalized pustular psoriasis was treated with isotretinoin, despite the known teratogenic effects of acitretin. Excellent result was noted in this young girl.<sup>56</sup>

#### *Methotrexate*

When the childhood psoriasis becomes severe and extensive (PASI $\geq$ 10) then the use of methotrexate is an effective option. Methotrexate has been widely used since decades in all moderate to severe types of childhood psoriatic patients and found

excellent results by giving the dose 0.2 to 0.7 mg/kg/ per week.<sup>55</sup> Due to lesser side effects than other available systemic treatments, physicians prefer to use this drug. Methotrexate has also the advantage over cyclosporin in managing the psoriatic arthritis. Initial dose may be started from 7.5mg per week. When the methotrexate was administered in 10 children with severe plaque psoriasis, the complete clearance was found in 80% patients, while 10% cases showed no response.<sup>57</sup> In a study from India carried out in 7 patients, the authors observed that 75% lesions clear with minimal scaling and erythema after using methotrexate for 6 to 10 weeks.<sup>58</sup> A complete remission was observed in pustular psoriasis children after giving the treatment for 4 to 12 weeks.<sup>59,60</sup>

#### *Biologics*

The biologics like etanercept, infliximab, tumor necrosis factor alpha (TNF- $\alpha$ ) inhibitor therapies have been used recently in pediatric autoimmune diseases like rheumatoid arthritis, TNF- $\alpha$  receptor 1-associated periodic syndrome without fever (TRAPS), juvenile idiopathic arthritis and Crohn's disease. Safety and efficacy of etanercept therapy has been recognized in juvenile rheumatoid arthritis patients even it was continuously used for 8 years.<sup>61</sup> There are mixed reports regarding the improvement of psoriasis with biologic agents. In a placebo-controlled, randomized, double-blind trial, 211 children with plaque psoriasis were treated with once-weekly subcutaneous injections of etanercept (0.8mg/kg), with a maximum of 50 mg. At week 12, 27% of patients reached PASI 90, in contrast to 7% of patients treated with placebo.<sup>62</sup> One patient with plaque psoriasis had no improvement even after 8 months of treatment<sup>63</sup>; while, in other studies, three children with severe psoriasis have shown remarkable improvement with etanercept.<sup>64,65</sup> However, these drugs cannot be used frequently because of their

cost-effectiveness and unavailability in the third world countries.

### Conclusion

The incidence of childhood psoriasis is exactly unknown. There is no difference between male and female children and the child may get the disease at any time before the age of 18 years. Plaque-type psoriasis is the commonest, however the guttate, pustular, erythrodermic and rheumatoid types are may be seen in childhood psoriasis. The exact pathogenesis of the psoriasis is still unknown. But, it is a genetically determined disorder and various factors like overweight, respiratory tract infections, positive throat culture for group A ss-hemolytic streptococcus, frequency of emotional stress and psychological disturbances are considered having a role in aggravating the disease.

Regarding the treatment in childhood psoriasis, topical treatment with corticosteroids and vitamin D analogues (calcipotriene and calcitriol) seems to be effective in mild plaque type psoriasis. Dithranol (anthralin) is also effective topical treatment in some extent. NB-UVB shows good results in the treatment of plaque and guttate type psoriasis and has comparatively mild side effects were seen. The use of oral antibiotics is limited. Due to the divided opinion in different studies, the use of cyclosporin in childhood psoriasis may not be fully recommended. Similarly, due to the severe side effects of oral retinoids, they may be used with required precautions, despite their successful results in pustular and erythrodermic psoriasis. In our opinion, methotrexate is an effective treatment in moderate to severe type psoriasis and is comparatively safe mild side effects in compare to other systemic treatment options. The biologic treatment, though, these drugs are recently introduced and have shown the

successful management in couple of studies and long-term side effects and risks are not described, but, these drugs may not be frequently used because of cost effective and unavailability in third world countries.

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