

# Juvenile dermatomyositis in Thai children: Retrospective review of 30 cases from a tertiary care center

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## Abstract

**Background:** Juvenile dermatomyositis is a rare condition, but it is the most common idiopathic inflammatory myopathy in pediatric patients.

**Aim:** To study the clinical manifestations, investigations, treatment, clinical course, and outcomes of juvenile dermatomyositis in Thai children.

**Method:** This retrospective study included juvenile dermatomyositis patients treated at Siriraj Hospital, a 2,300-bed national tertiary referral center in Bangkok, Thailand, from 1994 to 2019.

**Results:** Thirty patients (22 females and 8 males) were included with a female to male ratio of 2.7:1. Median age at diagnosis was 5.1 years (range, 2.6-14.8 years). Median duration of illness before diagnosis was 6.5 months (range, 0.3-84.0 months). Acute and subacute onset occurred in the majority of patients. Presenting symptoms included muscle weakness in 27/30 (90%), skin rash in 26/30 (86.7%), muscle pain in 17/26 (65.4%), and arthralgia in 4/18 (22.2%) of patients. Dermatologic examination revealed Gottron's rash, heliotrope rash, and periungual telangiectasia in 25/30 (83.3%), 21/30 (70.0%), and 15/24 (62.5%) of patients, respectively. Interestingly, scalp dermatitis was found in 8/21 (38.1%) of patients. The most commonly used treatment regimen in this series was a combination of prednisolone and methotrexate. During the median follow-up of 3.1 years (range, 0.0-18.5 years), only one-third of patients were seen to have monocyclic disease. Extraskeletal osteosarcoma at a previous lesion of calcinosis cutis was observed in one patient at 12 years after juvenile dermatomyositis onset.

**Limitations:** This was a retrospective single-center study, and our results may not be generalizable to other healthcare settings. Prospective multicenter studies are needed to confirm the findings of this study.

**Conclusion:** juvenile dermatomyositis usually poses a diagnostic and therapeutic challenge, which can be compounded by the ethnic variations in the clinical presentation, as observed in this study. Asian patients tend to present with acute or subacute onset of disease, and arthralgia and/or arthritis are less common than in Caucasian patients. Scalp dermatitis is not uncommon in pediatric juvenile dermatomyositis patients. An association between juvenile dermatomyositis and malignancy, though rare, can occur.

**Key words:** Juvenile dermatomyositis, JDM, osteosarcoma, Thai, children, calcinosis cutis, pediatric

## Plain Language Summary

Dermatomyositis is an autoimmune disease, where the patient's immune system attacks the body's own tissues. It primarily affects skin and muscles. In this report we describe the symptoms, clinical examination findings and results of investigations in 30 children with dermatomyositis, seen over 25 years at one large hospital in Thailand. Quick progression of the illness

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was common in our patients. Involvement of joints was less common than in Caucasian patients. Early and aggressive treatment can control this disease. One of our patients developed a form of cancer in an area of abnormal calcium deposition. Dermatomyositis in children is rare and we hope our findings will be useful to other physicians.

## Introduction

Juvenile dermatomyositis is quite rare, but it is the most common idiopathic inflammatory myopathy in pediatric patients.[1] Juvenile dermatomyositis is characterized by proximal muscle weakness, characteristic rashes, and vasculopathy. The incidence of juvenile dermatomyositis is estimated to be about 2-4 per one million children, with differences among racial and ethnic groups.[2-6]

Skin manifestations are a key feature of juvenile dermatomyositis, and they may precede, accompany or follow the onset of muscle weakness. According to the 2017 EULAR/ACR classification criteria for idiopathic inflammatory myopathy, juvenile dermatomyositis can be diagnosed with high sensitivity and specificity in the presence of three cardinal skin signs, including heliotrope rash, Gottron's papules, and Gottron's sign.[7] Heliotrope rash, a purplish-red erythema on the eyelids, is found in 70-100% of patients.[1,5,8-14] Flat-topped, violaceous papules (Gottron's papules) and telangiectatic erythema (Gottron's sign) over the knuckles and interphalangeal joints are pathognomonic signs of juvenile dermatomyositis with a reported prevalence of 56-96%.[1,5,8-12,14] Scalp erythema with or without scaling resembling seborrheic dermatitis, periungual telangiectasia, and cuticular changes have all been described in patients with juvenile dermatomyositis.[8,11,15] Several other cutaneous features can also be observed, including malar erythema, poikiloderma, vasculitic lesions, cutaneous ulceration, lipodystrophy, calcinosis cutis, and nailfold capillary changes.[16,17]

Symmetrical proximal muscle weakness is the hallmark feature of juvenile dermatomyositis. Arthralgia and arthritis are also often observed. Involvement of other systems is occasionally found, including the lungs, heart, and gastrointestinal tract, and these types of systemic involvement may have a major impact on disease course and prognosis.

Among patients for whom a diagnosis of juvenile dermatomyositis is being considered, thorough history taking, physical examination, and laboratory studies should be performed to obtain a baseline disease evaluation, assessment of severity, monitoring, prognosis and identification of associated disorders. Myositis-specific antibodies are increasingly used as diagnostic and prognostic markers in juvenile dermatomyositis patients, and they can be identified in 60-95% of patients with juvenile dermatomyositis.[18-21] The approach to diagnosis of juvenile dermatomyositis has changed with decreased use of electromyography (EMG) and muscle biopsy, both of which are invasive procedures. Magnetic resonance imaging (MRI) can be used to assess inflammation in muscles in order to localize the affected area for biopsy, for diagnosis, and for monitoring disease activity.[21,22] Despite the gradually increasing use of MRI in developed countries around the world, it is used much less often in developing countries since it is expensive and often not available.

Treatment in juvenile dermatomyositis aims to control inflamed muscles, improve skin lesions, prevent organ damage, and treat complications. Treatment must be started early and requires a multidisciplinary team. Given the scarcity of juvenile dermatomyositis-specific data in Thailand, the aim of this study was to identify the clinical characteristics, investigation findings, treatment modalities, clinical course and outcomes of juvenile dermatomyositis in Thai children.

## Methods

This retrospective study was conducted at the Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, a national tertiary care hospital in Bangkok, Thailand. The study protocol was approved by the Siriraj Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (COA no. Si 479/2008). The requirement to obtain written informed consent was waived due to the retrospective nature of this study.

### Patient selection

Juvenile dermatomyositis patients seen during January 1994 to November 2019 who were aged <18 years at disease onset and who satisfied the Bohan and Peter criteria for classification[23,24] as definite juvenile dermatomyositis were included.

### Retrospective assessment

The following information was collected from the medical records: demographic data, age of onset, age at diagnosis, onset type (progression of the first symptoms to the presentation that fulfilled Bohan and Peter criteria, and characterized as acute if it occurred within one month, subacute if it occurred in 1-3 months, and insidious if it took longer than three months), clinical features, results of investigations, treatment, complications, and outcomes. Disease course was classified as *monocyclic* if the patient had full recovery within one year after initiation of therapy without any relapse, *chronic polycyclic* in cases of relapsing-remitting disease, and *chronic continuous* if the patient had persistent active disease for more than one year after diagnosis.[10] Due to the retrospective design of this study, the results described in medical record were reported.

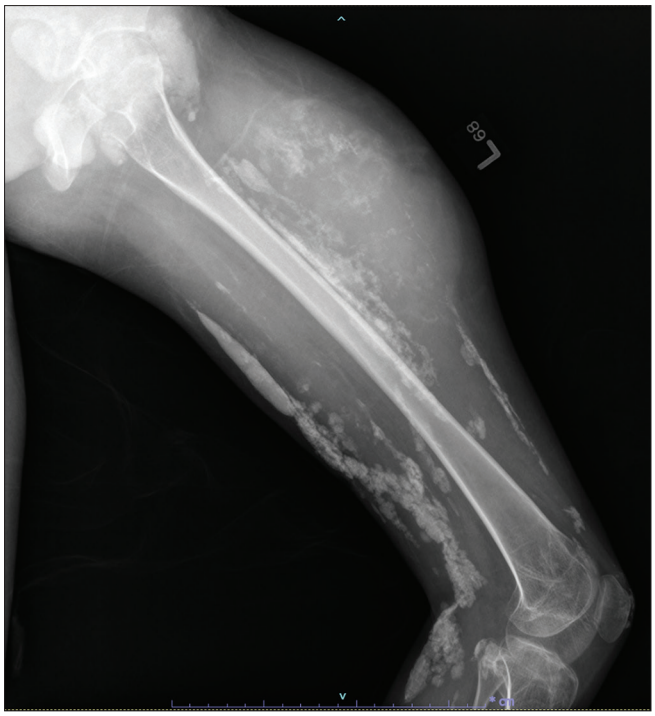

**Figure 1:** Huge soft tissue mass at left proximal thigh with internal amorphous calcifications. Femoral cortex preserved.

### Statistical analysis

Descriptive statistics are expressed as frequency and percentage for categorical variables, as mean ± standard deviation for normally distributed quantitative continuous variables, and as median and range [interquartile range (IQR) or minimum to maximum] for non-normally distributed quantitative continuous variables. Chi-square test, Fisher's exact test, or independent-samples *t*-test was used to determine differences between groups. A *p*-value less than 0.05 was considered statistically significant. SPSS Statistics software (SPSS, Inc., Chicago, IL, USA) was used to perform all statistical analyses.

## Results

### Demographic data

Thirty cases (22 females and 8 males) diagnosed with definite juvenile dermatomyositis were enrolled in this study. Forty percent of patients presented with their first symptoms at an age less than five years. The median duration from initial symptoms to fulfilling Bohan and Peter criteria was two months (range: 0.5-24 months). No patient had a family history of juvenile dermatomyositis or other connective tissue diseases.

### Clinical manifestations

The most common presenting complaints were weakness, rash, and muscle pain in 27/30 (90%), 26/30 (86.7%), and 17/26 (65.4%) of patients, respectively [Table 1]. From patient history, 10 (33.3%) and 11 (36.7%) of patients presented with a rash that occurred before and concomitant with muscle weakness, respectively. In this study, most patients (27/30, 90%) had muscle weakness. Proximal muscle weakness

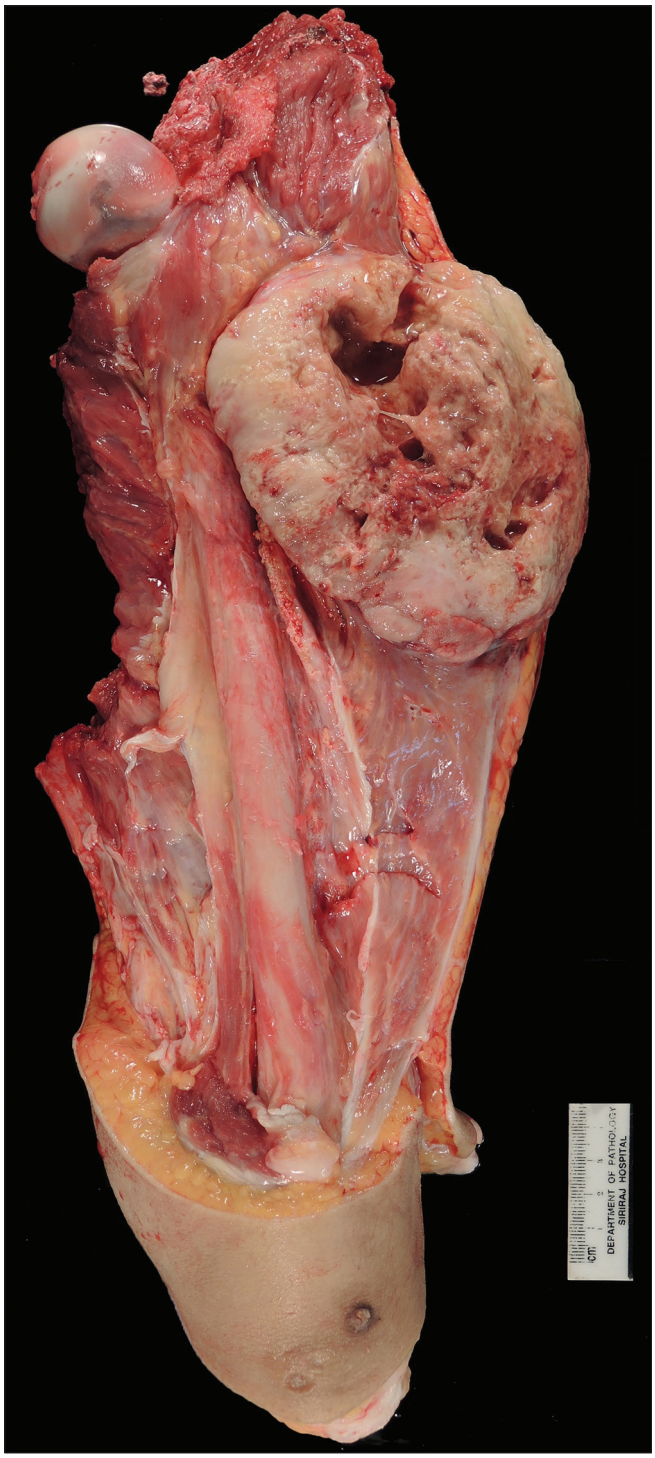


**Figure 2:** Huge deep-seated soft tissue mass at anterolateral aspect of left proximal thigh with heterogeneous tan-white tumor tissue, gritty calcifications, tumor necrosis, and cystic change. No femoral cortex invasion.

affecting the limb-girdle and/or the neck flexor muscles accounted for most of the presenting symptoms in patients with muscle weakness. There was no case of amyopathic dermatomyositis in this study. There were 3 (10%) cases without clinically significant muscle weakness; however, all of those three patients had classic cutaneous features,

**Table 1. Demographic and clinical characteristics of juvenile dermatomyositis patients compared among studies[1,5,8-14]**

| Characteristics | This study 2021 Thailand (N=30) | *Singalavanija* 2001 Thailand (N=7) | McCann 2006 UK & Ireland (N=151) | Ravelli 2010 International multicenter (N=490) | Prasad 2013 India (N=18) | Gowdie 2013 Australia (N=57) | Shah 2013 Collaborative study group (N=354) | Sun 2015 Taiwan (N=39) | Barut 2017 Turkey (N=50) | Sharma 2020 India (N=37) |
|---|---|---|---|---|---|---|---|---|---|---|
| | Median | Mean | Median | Mean | Median | Median | Median | Mean | Mean | Median |
| Age at diagnosis (yrs) | 5.1 (2.6-14.8) | N/A | 7 (1-16) | N/A | 12.5 (2.5-16) | 7.1 (2.2-15.3) | 7.4 (5.1-11.3) | 7.3 (2.3-17.8) | 6.6 (2.0-16.0) | 6 (1.5-14) |
| Age at onset (yrs) | 4.1 (0.6-14.3) | 7 (2.5-11) | N/A | 6.9 (0.9-17.8) | N/A | N/A | 6.9 (4.5-10.6) | 7.3 (2.1-12) | 6.1 (1.5-16.0) | N/A |
| Duration of illness before diagnosis (months) | 6.5 (0.3-84.0) | N/A | 3 (1.0-118.0) | N/A | 9.25 (0.5-120) | 2.8 (0.7-20.5) | 4 (2.0-7.8) | 6.1 (0-24) | N/A | 5 (0.36) |
| Female gender, n (%) | 22 (73.3%) | 6 (85.7%) | 104 (68.8%) | 321 (65.5%) | 9 (50.0%) | 38 (67.0%) | 258 (72.9%) | 36 (66.7%) | 35 (70.0%) | 18 (48.6%) |
| Disease onset, n (%) | | | | | | | | | | |
| Acute (<1 month) | 4 (13.3%) | N/A | N/A | 279 (57.0%) * | N/A | N/A | 41 (11.7%) | N/A | N/A | N/A |
| Subacute (1-3 months) | 14 (46.7%) | N/A | N/A | N/A | N/A | N/A | 90 (25.8%) | N/A | N/A | N/A |
| Insidious (>3 months) | 11 (36.7%) | N/A | N/A | 211 (43.0%) ** | N/A | N/A | 218 (62.5%) | N/A | N/A | N/A |
| Presenting symptoms, n (%) | | | | | | | | | | |
| Muscle weakness | 27/30 (90.0%) | 6 (85.7%) | 121 (82.0%) | 416 (84.9%) | 17 (94.4%) | 54/57 (95.0%) | 353 (99.8%) | 32 (82.1%) | 45 (90.0%) | 37 (100%) |
| Cutaneous/Gottron's rash | 26/30 (86.7%) | 4 (57.1%) | 132 (88.0%) | 357 (72.9%) | 14 (77.7%) | 51 (91.0%) | 356 (81.8%) | 32 (81.1%) | 48 (96.0%) | 32 (86.4%) |
| Muscle pain | 17/26 (65.4%) | 2 (28.0%) | 98 (68.0%) | N/A | N/A | 46/51 (90.0%) | 208 (60.5%) | 7 (18.0%) | N/A | N/A |
| Arthralgia/arthritis | 4/18 (22.2%) | N/A | 98 (66.0%) | 175 (35.7%) | 6 (33.3%) | 15/43 (35.0%) | 150 (42.5%) | 7 (18.0%) | N/A | 4 (10.8%) |
| Joint deformity | 3/18 (16.6%) | N/A | 38 (27.0%) | 82 (18.3%) | N/A | 17/29 (59.0%) | N/A | N/A | N/A | N/A |
| Fatigue | 9/20 (45.0%) | N/A | N/A | N/A | N/A | N/A | 303 (85.8%) | N/A | N/A | N/A |
| Fever | 8/20 (26.7%) | N/A | N/A | N/A | N/A | 16/45 (36.0%) | 139 (39.3%) | N/A | N/A | N/A |
| Poor appetite | 6/21 (28.6%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Weight loss | 6/22 (27.3%) | N/A | N/A | N/A | N/A | 25/41 (61.0%) | 125 (35.6%) | N/A | N/A | N/A |
| Hepatomegaly | 4/30 (13.3%) | N/A | N/A | N/A | N/A | 5/41 (12.0%) | N/A | N/A | N/A | N/A |
| Diarrhea | 2/25 (8.0%) | N/A | N/A | N/A | N/A | N/A | 36 (10.2%) | N/A | N/A | N/A |
| Swallowing difficulty | 2/29 (6.9%) | N/A | 33 (29.0%) | N/A | 4 (22.2%) | 11/44 (25.0%) | 139 (39.4%) | 4 (10.3%) | N/A | N/A |
| Dyspnea | 1/29 (3.4%) | N/A | 23 (18.0%) | N/A | N/A | N/A | 39 (11.1%) | N/A | N/A | N/A |
| Horseness/dysphonia | 1/29 (3.4%) | N/A | 22 (17.0%) | N/A | 2 (11.1%) | 14/31 (45.0%) | 106 (30.2%) | N/A | N/A | N/A |

*Acute: high fever, prostration, rash, and profound muscle weakness

**Insidious: progressive development of muscle weakness and rash

Abbreviation: N/A, not available

abnormal muscle enzymes, EMG, and/or relevant changes on muscle biopsy.

The cutaneous findings observed in our patients are shown in Table 2. Thirty percent of patients who reported pigmentary changes had post-inflammatory hypo- or hyperpigmentation after resolution of active cutaneous lesions. We did not find any poikilodermatous changes.

Constitutional symptoms, such as fever, weight loss and poor appetite were found in less than 30% of patients. Gastrointestinal involvement included hepatomegaly, diarrhea, and swallowing difficulty, in 4/30 (13.3%), 2/25 (8%) and 2/29 (6.9%) of patients respectively. We found only 1/29 (3.4%) of patients presenting with dysphonia and dyspnea.

### Investigations

The results of related investigations are shown in Table 3. EMG in 11 of 13 (84.6%) patients revealed myopathic changes and muscle membrane irritability consistent with inflammatory myopathy. Muscle biopsy was performed in 19 cases, and 17 of them (89.5%) demonstrated mononuclear cell infiltration in the perimysium and blood vessels with extension into perifascicular muscle fibers, and coexisting perifascicular atrophy. MRI was performed in only two cases, both of which showed muscle swelling and atrophy consistent with myositis. Myositis-specific antibodies testing was performed in 18 cases. Of those, 5 (27.8%) patients were positive, with one each of anti-nuclear matrix protein 2 (NXP2) antibody, anti-melanoma differentiation-associated protein 5 (MDA5) antibody, anti-Ku, anti-Jo1 and anti-signal recognition particle (SRP) antibody.

### Treatment

Rashes were treated with topical corticosteroids in most (19/20, 95%) patients, and low to moderate potency topical corticosteroids were used in most (18/19, 94.8%) of these. Topical calcineurin inhibitors were prescribed in 5/20 (25%) of patients (pimecrolimus in 5%, and tacrolimus in 20%). Photoprotection and sunscreens were recommended in all patients.

Systemic corticosteroids were the mainstay of therapy (26/27, 96.3%), and 22.2% of patients received corticosteroids monotherapy. Pulse intravenous methylprednisolone (30 mg/kg/dose) for 1-3 days was prescribed initially in

**Table 2. Cutaneous manifestations of juvenile dermatomyositis compared among studies[5,8-15]**

| Manifestations | This study 2021 Thailand (N=30) | *Singalavanija* 2001 Thailand (N=7) | Peloro 2001 Pennsylvania, USA (N=16) | Ravelli 2010 International multicenter (N=490) | Prasad 2013 India (N=18) | Gowdie 2013 Australia (N=57) | Shah 2013 Collaborative study group (N=354) | Sun 2015 Taiwan (N=39) | Barut 2017 Turkey (N=50) | Sharma 2020 India (N=37) |
|---|---|---|---|---|---|---|---|---|---|---|
| Gottron's papules/sign | 25/30 (83.3%) | 2 (28.5%) | 9 (56.3%) | 357 (72.9%) | 14 (77.7%) | 51/56 (91.0%) | 320 (90.7%) | 32 (82.1%) | 48 (96.0%) | 30 (81.1%) |
| Heliotrope rash | 21/30 (70.0%) | 6 (85.7%) | 10 (62.5%) | 304 (62.0%) | 10 (55.5%) | 36/49 (73.0%) | 305 (86.7%) | 29 (74.4%) | 50 (100%) | 32 (86.4%) |
| Periungual capillary changes* | 15/24 (62.5%) | N/A | 12 (75.0%) | N/A | N/A | 26/38 (68.0%) | 271 (78.8%) | N/A | N/A | N/A |
| Photosensitivity | 13/25 (52.0%) | 2 (28.5%) | N/A | N/A | N/A | N/A | 160 (46.9%) | 3 (7.7%) | N/A | N/A |
| Telangiectasia** | 9/19 (47.4%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Malar rash | 13/30 (43.3%) | N/A | 9 (56.3%) | 278 (56.7%) | N/A | 30/38 (79.0%) | 26 (73.7%) | 22 (56.4%) | N/A | N/A |
| Scalp dermatitis*** | 8/21 (38.1%) | N/A | 4 (25.0%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Pruritus | 7/22 (31.8%) | N/A | 6 (38.0%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Pigmentary changes | 7/23 (30.4%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Vasculitic skin lesions**** | 7/24 (29.2%) | N/A | N/A | N/A | N/A | N/A | N/A | 1 (2.6%) | N/A | N/A |
| Palmar erythema | 6/22 (27.2%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Calcinosis cutis | 6/28 (21.4%) | 4 (57.1%) | 2 (13.0%) | 106 (23.6%) | 5 (27.8%) | 0/13 (0.0%) | N/A | 15 (38.5%) | 19 (38.0%) | 4 (10.8%) |
| Ulcer***** | 6/29 (20.7%) | N/A | 1 (6.0%) | N/A | N/A | 3/13 (23.0%) | 71 (20.2%) | 1 (2.6%) | N/A | N/A |
| Edema of the feet | 4/24 (16.7%) | N/A | N/A | N/A | N/A | N/A | 54 (15.3%) | N/A | N/A | N/A |
| Livedo reticularis | 3/26 (11.5%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Non-scarring alopecia | 2/26 (7.7%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Hirsutism | 1/21 (4.8%) | N/A | N/A | 44 (10.2%) | N/A | N/A | N/A | N/A | N/A | N/A |
| Lipodystrophy | 1/29 (3.4%) | N/A | N/A | 43 (9.7%) | 2 (11.1%) | N/A | 35 (9.9%) | N/A | N/A | N/A |
| Mechanic's hand | 0/30 (0.0%) | N/A | N/A | N/A | 1 (5.5%) | N/A | 26 (7.5%) | N/A | N/A | N/A |

Data presented as number and percentage

*Periungual capillary changes included periungual telangiectasia, nailfold capillary loop dilatation and drop out.

**Telangiectasia presented on the skin such as the periorbital area, cheeks, chest and back. Not included periungual telangiectasia.

***Scalp dermatitis is defined as scalp erythema with or without scaling resembling seborrheic dermatitis.

****Vasculitic lesions included telangiectatic lesions, erythematous to purplish macules and papules on acral areas, and cutaneous ulceration

*****Ulcers in this study were mostly caused by protruded calcinosis cutis. Some of the patients developed ulcers from lipodystrophy and panniculitis. Not included cutaneous ulcers from vasculitic lesions.

Abbreviation: N/A, not available

13 (48.1%) of 27 patients with severe clinical presentations such as severe myositis or respiratory involvement, and that treatment was followed by tapered oral prednisolone. The median initial prednisolone dose was 2 mg/kg/day (range, 0.4-2 mg/kg/day). Twenty-one (77.8%) of 27 patients were concurrently started on additional immunosuppressive medications. A combination of prednisolone and methotrexate was the most common regimen used (20 patients, 74%), with a mean methotrexate dose of 0.5 ± 0.1 mg/kg/week. Cyclophosphamide was used in three patients, two with respiratory failure from rapidly progressive interstitial lung disease, and one patient with refractory weakness and dermatitis despite a combination of immunosuppressive agents including prednisolone, azathioprine and cyclosporin. Other immunosuppressive drugs included mycophenolate mofetil (5/27, 18.5%), intravenous immunoglobulin (3/27, 11.1%), cyclosporin (1/27, 3.7%) and azathioprine (1/27, 3.7%). Antimalarial drugs were used in 18/27 (66.7%) patients. Hydroxychloroquine was the most commonly used anti-malarial with an average dosage of 4.5 ± 0.7 mg/kg/day.

### Clinical outcomes, complications, and course of disease

The mean follow-up period was 3.1 years (range, 0-18.5 years). Three of the patients were followed up less than 1 years. The disease course of 30 patients was classified as monocyclic, chronic polycyclic, and chronic continuous type in 9 (33.0%), 8 (26.7%), and 7 (23.3%) patients, respectively. The disease course in this study and in other published studies is presented in Table 4. Serum alanine aminotransferase, aspartate aminotransferase, creatine kinase values returned to their normal levels in mean durations of 1.1, 1.5, 1.6, and 9.3 months respectively, after the start of treatment.

Side effects of systemic and topical corticosteroids were detected in 12/24 (50%) of patients, including cushingoid appearance (8/24, 33.3%), acneiform eruption (4/23, 17.4%), cataract (3/23, 13%), osteoporosis (2/23, 8.7%), and glaucoma (1/23, 4.4%). One patient developed severe osteoporosis and vertebral compression fracture. No patients developed other connective tissue diseases or overlap syndromes during the follow-up period. Side effects of immunosuppressive drugs were mostly transient hepatitis (one patient) and renal insufficiency (one patient, three years after receiving methotrexate). After discontinuation of the medication, all the abnormalities returned to be normal. One patient developed methotrexate-induced liver fibrosis confirmed by fibroscan.

**Table 3. Investigation results in Thai juvenile dermatomyositis patients (N=30)**

| Investigation results | Number of abnormal results/ total number tested (%) | Normal value | Mean | Range |
|---|---|---|---|---|
| Muscle biopsy | 17/19 (89.5%) | - | - | - |
| Electromyography | 11/13 (84.6%) | - | - | - |
| Abnormal muscle enzymes | 30/30 (100%) | | | |
| Elevated lactate dehydrogenase | 29/29 (100%) | 120-300 U/L | 878.0 | 389-2473 |
| Elevated aspartate aminotransferase | 22/22 (73.3%) | 0-40 U/L | 108.9 | 13-551 |
| Elevated creatine kinase | 21/30 (70.0%) | 0-170 U/L | 1258.2 | 39-14410 |
| Elevated alanine aminotransferase | 14/30 (46.7%) | 0-41 U/L | 62.9 | 12-371 |
| Complete blood count | | | | |
| Thrombocytosis | 23/27 (76.7%) | 150000-350000 cells/uL | 312571.4 | 128000-657000 |
| Anemia | 12/29 (41.4%) | 11.5-13.5 g/dL | 11.6 | 7.4-14.7 |
| Inflammatory markers | | | | |
| Elevated erythrocyte sedimentation rate | 19/28 (67.9%) | 0-15 mm/hr | 34.2 | 3-115 |
| Elevated C-reactive protein | 5/15 (33.3%) | < 5 mg/L | 3.2 | 0.6-10.7 |
| Radiologic study | | | | |
| Muscle magnetic resonance imaging | 2/2 (100%) | - | - | - |
| Soft tissue film | 5/7 (71.4%) | - | - | - |
| Autoantibody | | | | |
| Antinuclear antibody | 12/27 (44.0%) | - | - | - |
| Myositis-specific antibodies | 5/18 (27.8%) | - | - | - |
| Cardiac evaluation | | | | |
| Echocardiography | 0/5 (0.0%) | - | - | - |
| Electrocardiography | 0/12 (0.0%) | - | - | - |
| Other studies | | | | |
| Pulmonary function test | 3/8 (37.5%) | - | - | - |
| Abnormal lipid profile | 1/5 (20.0%) | - | - | - |

**Table 4. Disease course of juvenile dermatomyositis compared among studies[8-12,14,25,26]**

| Disease course | 2021 Thailand (N=30)** | Stringer 2008 Canada (N=84) | Ravelli 2010 International multicenter group (N=490) | Patwardhan 2012 USA (N=78) | Prasad 2013 India (N=18) | Gowdie 2013 Australia (N=57) | Shah 2013 Collaborative study group (N=354) | Sun 2015 Taiwan (N=31) | Sharma 2020 India (N=37) |
|---|---|---|---|---|---|---|---|---|---|
| | Median | Median | Mean (min-max) | Mean | Median | Median | Median | N/A | Median |
| Follow-up period (yrs) | 3.1 (0.0-18.5) | 5 (0.3-14) | 7.7 (2-25.2) | Age onset ≤3 yrs: 78.4±61 mo<br>Age onset >3 yrs: 95.1±22.1 mo | 2 | 4 | 4.4 (2.2-7.7) | N/A | 5 (2-18.2) |
| | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| | 1 yr of diagnosis | 3 yrs follow-up | 2 yrs of diagnosis | *4 yrs follow-up | Not clarified | 3 yrs of diagnosis | 2 yrs of diagnosis | Not clarified | 2 yrs of diagnosis |
| Monocyclic | 9 (30.0%) | 23 (37.0%) | 198 (41.3%) | 36 (46.2%) | 11 (61.2%) | 21/45 (46.7%) | 71 (24.5%) | 6 (19.4%) | 26 (70.3%) |
| Chronic polycyclic | 8 (26.7%) | 2 (3.0%) | 281 (58.7%) | 22 (28.2%) | 5 (27.8%) | 8/45 (17.7%) | 73 (25.2%) | 25 (80.6%) | 8 (21.6%) |
| Chronic continuous | 7 (23.3%) | 37 (60.0%) | | 20 (25.6%) | 1 (5.5%) | 16/45 (35.5%) | 146 (50.3%) | | 3 (8.1%) |
| Death | 3 (10.0%) | N/A | 15 (3.1%) | N/A | 1 (5.5%) | N/A | 8 (2.4%) | 2 (5.1%) | N/A |

*Monocyclic: single episode of the disease with only one remission and no relapses; Chronic polycyclic: more than one remission and relapse in the disease course of any duration; Chronic continuous: continuously active disease course without definite remissions

** Three patients in this study were followed up less than 1 year after diagnosis.

Abbreviation:N/A, not available

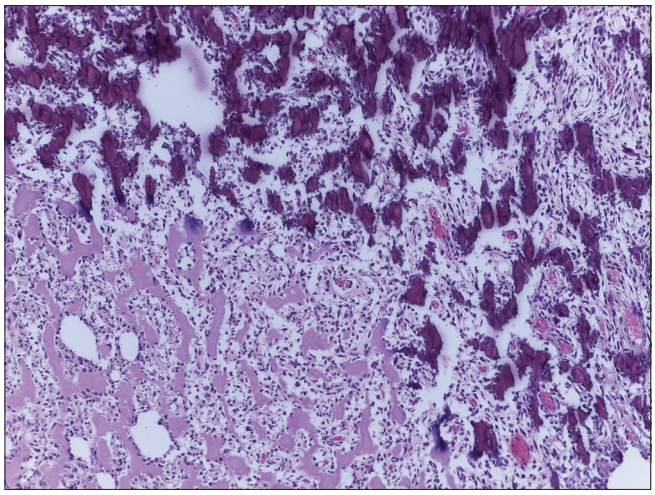

**Figure 3:** The tumor is composed of spindle and polygonal cells producing trabecular osteoid (left lower) and bone matrix (right upper). (H&E, 100x)

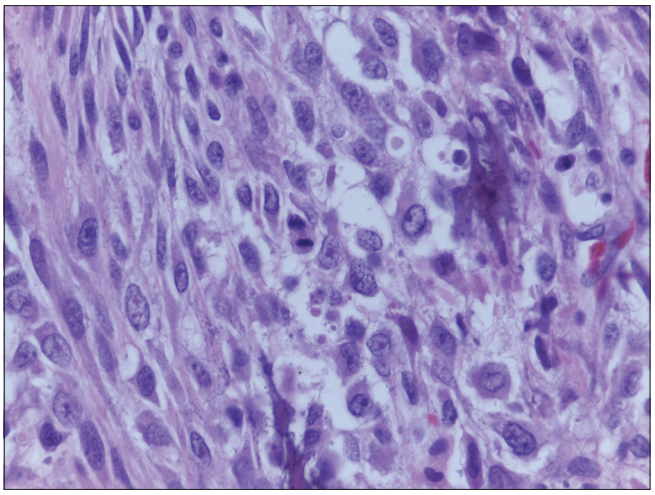

**Figure 4:** The tumor cells contain enlarged atypical nuclei with coarse chromatin and prominent nucleoli. Mitotic figures are frequently observed. (H&E, 600x)

Calcinosis cutis was found in 6/28 (21.4%) of juvenile dermatomyositis patients, and statistically strongly correlated with increased duration of illness before diagnosis ($p$=0.008). Those with calcinosis cutis had had their illness for a median duration of 1.8 years (range, 0.6-6 years) before diagnosis. In contrast, patients who did not have calcinosis cutis had their illness for a median duration of only 0.45 years (range, 0.06-7 years) before diagnosis. Two patients with calcinosis cutis received bisphosphonate therapy. One of those patients improved after two courses of pamidronate, but the other patient was given both diltiazem and pamidronate and had no significant improvement. Extraskeletal osteosarcoma in long-standing calcification was observed in one of the six patients with calcinosis cutis in this study. The diagnosis was made 12 years after disease onset. At the time of diagnosis, she had already developed multiple calcified lesions that resulted in flexion contractures of the elbows, and metacarpophalangeal and interphalangeal joints of the hands. Despite aggressive treatment including intravenous pulse methylprednisolone, oral prednisolone and methotrexate, her disease intermittently relapsed. Calcinosis cutis was treated with diltiazem and bisphosphonate for one year, but there was no improvement; only progression was observed. Twelve years after disease onset, she developed a progressively enlarging mass at the left thigh. Soft tissue X-ray of the thighs showed a huge soft tissue mass with internal amorphous calcifications [Figure 1]. Tissue biopsy revealed a high-grade extraskeletal osteosarcoma without vascular or nerve invasion [Figures 2, 3, and 4]. Left hip disarticulation was then performed. This patient continues to be treated for juvenile dermatomyositis and wears a limb prosthesis.

Three (16.6%) of 18 patients presented with joint deformity at the time of diagnosis. The elbow and knee joints were the common sites of joint contracture in the patients. One of our patients also involved the small joints of the hands including metacarpophalangeal and proximal interphalangeal joints. The mean duration of illness before diagnosis in these patients was 1.8±0.9 years. Joint deformity was found to be significantly correlated with abnormal muscle enzyme levels ($p$=0.02).

The mortality rate was 11.1% (3/30 patients) in this study. One patient died from respiratory failure despite aggressive therapy including pulse methylprednisolone, and intravenous immunoglobulin. Two severe juvenile dermatomyositis cases had respiratory failure and were treated with pulse intravenous cyclophosphamide (500 mg/m$^2$/dose), and one of those patients received extracorporeal membrane oxygenation (ECMO) and plasmapheresis. Ultimately, both of those patients succumbed to sepsis and aspiration pneumonia.

## Discussion

Data from our cohort are compared with with data from previously reported juvenile dermatomyositis cohorts in Tables 1[1,5,8-14], 2[5,8-15] and 4[8-12,14,25,26].

Our cohort had substantially more females than males, which is similar to findings in several other reports.[1,5,8-14] The median age of onset in juvenile dermatomyositis patients was 6 to 7 years of age in most studies.[5,10,11,13,14] However, the median age of onset in this study was 4.1 years. Disease onset in juvenile dermatomyositis is quite variable. The majority (60%) of our study population presented with an acute or subacute onset. A collaborative study by Shah, *et al*. found insidious onset of disease in 62% of their patients.[11] All of our patients were of Asian ethnicity, but 71.2% of those collaborative study patients were Caucasians; the observed differences in disease onset pattern may be due to different ethnicities. Clinical manifestations also may vary among populations. Arthralgia and/or arthritis were more common in Caucasian populations (35.7-66%)[1,8,10,11] than in Asian populations (10.8-33.3%).[9,12,14]

The median duration of illness before diagnosis was 6.5 months in the present study. This figure has ranged

from 5 to 9.3 months in developing countries,[9,12,14] while in developed countries it was only 2.8-4.0 months.[1,8,11] Possible explanations for this difference may be higher educational and income levels, easier access to testing and early referral in developed countries.

Our study focused on cutaneous manifestations in Thai juvenile dermatomyositis patients. Common findings in our study and other studies were Gottron's rash, heliotrope rash, and periungual capillary changes.[5,8-15] Scalp dermatitis was seen in 38% of our patients, so we recommend that careful scalp evaluation be included as a component of physical examination of patients suspected to have juvenile dermatomyositis. Importantly, vasculitic skin lesions, which are not described as common in juvenile dermatomyositis patients, presented in 25% of our patients.

Our data revealed lactate dehydrogenase (LDH) to be the most sensitive marker for juvenile dermatomyositis; all patients with elevated LDH were accurately diagnosed with juvenile dermatomyositis despite no apparent muscle weakness in some of them. Elevated erythrocyte sedimentation rate and thrombocytosis was found in 76.7% and 67.9% of our patients, respectively; these parameters may also be useful markers of disease activity.

Muscle biopsy and electromyography have high sensitivity for diagnosis of juvenile dermatomyositis, and they showed positive results in 89.5% and 84.6% of our patients respectively. Myositis-specific antibodies are also valuable markers that can predict phenotypes, histopathological correlations, and prognosis.[27-29] However, these correlations were not significantly detected in our study since these antibodies were positive in only a minority of patients.

The most common initial glucocorticoid therapy in our patients was pulse methylprednisolone and moderate- to high-dose daily corticosteroids. A combination of prednisolone and methotrexate was the maintenance treatment regimen most often prescribed for our study patients. This regimen was more effective than prednisolone alone in a previous study, and it showed evidence of a better safety profile than prednisolone combined with other immunosuppressive drugs.[30]

The disease course described in juvenile dermatomyositis has varied across studies.[8-12,14,25,26] Except for studies from India, the majority (53.2-80.6%) of patients had a relapsing-remitting or chronic continuous course.[8,10,11,14,25,26] Similarly, our study found that 50% of patients had recurrence of active disease or persistent disease. Only 30% of our patients achieved disease remission without evidence of active disease within one year of diagnosis. Among several reports, the frequency of a monocyclic disease course varied from 19.4% to 46.2%.[8,10,11,14,25,26] This difference among studies may be due to variations in the definitions of the duration of treatment to achieve remission after initiation of therapy to classify the course of the disease.

Malignancies, particularly lymphoma, have been rarely reported to be associated with juvenile dermatomyositis.[31-33] The case of osteosarcoma arising within calcification of dermatomyositis found in this study is extremely rare. We found only one case report (Mayo Clinic, 1981) describing a 32-year-old man who progressively developed extensive calcinosis cutis from 3 or 4 years of age.[34] He developed a rapidly enlarging mass at the left thigh which was diagnosed as a high-grade osteosarcoma. Considering that there are now two reports of juvenile dermatomyositis patients with osteosarcoma, the association between osteosarcoma and juvenile dermatomyositis may not be a coincidence. Malignant transformation of benign extraskeletal osseous tissue to osteosarcoma can occur on long-standing and extensive calcinosis cutis.[34] The fact that both patients developed osteosarcoma at the thigh should heighten clinicians' suspicion for abnormal activity at the thigh in juvenile dermatomyositis with calcinosis cutis.

The 10% mortality rate in this study was higher than in previous studies (2.4-5.5%).[9-11,14] Respiratory involvement and infectious complications were the causes of death in juvenile dermatomyositis patients in this study, which is similar to previous studies.[6,35,36]

### Limitations

The retrospective design of our study renders it vulnerable to incomplete or missing data. Second, this was a single-center study. Third, our center is Thailand's largest national tertiary referral center, and our findings may not be generalizable to other care settings. Finally, our sample size was small due to the relative rarity of this disease. Future prospective multicenter studies and/or meta-analyses are needed.

## Conclusion

The results of this study provide a broad profile of juvenile dermatomyositis in Thailand. Asian patients tend to present with acute or subacute onset and less arthralgia/arthritis compared to Caucasians. The duration of illness before diagnosis of juvenile dermatomyositis was longer than in developed countries, likely due to lower literacy and limited resources. Vasculitic skin lesions were not uncommon; awareness of this presentation is important. In patients with long-standing and extensive calcinosis cutis, physicians should look out for the development of extraskeletal osteosarcoma.

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**Conflicts of interest**

There are no conflicts of interest.

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