

SPECIAL ARTICLE ON REGIONAL PEDIATRIC RHEUMATOLOGY

Pediatric Rheumatology in Asia: The Thai Experience

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INTRODUCTION

The Kingdom of Thailand lies in the heart of Southeast Asia. The size of the country is 514,000 sq. km. or slightly more than twice the size of Wyoming in the United States. The population is 64 million (July 2003 estimate). Children younger than 15 years are comprise 24% of the population. There are five major medical schools in Thailand, with two based in the capital, Bangkok. Mahidol University is the largest.

Thailand did not have a pediatric rheumatologist or pediatric rheumatology division until January 2001 when the first pediatric rheumatology division was established at the Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University in Bangkok. Prior to this time, children with pediatric rheumatic disease were evaluated and treated by multiple pediatric subspecialists. The Department of Pediatrics at Siriraj Hospital recruited the author in 2001 as part of a pediatric department development plan to address a need for a clinical rheumatologist and immunologist as I have American board certification in allergy/ immunology and pediatric rheumatology. The following article presents a current assessment of the pediatric rheumatic diseases seen in Thailand in 2001-2003 and the treatment available for the children with rheumatic disease in Thailand during this period.

METHODS AND RESULTS

DISEASE PREVALENCE

After the pediatric rheumatology division was established in early 2001, Siriraj Hospital became the tertiary referral center for children with rheumatologic conditions from other tertiary care centers around the country. During a two-year period, 300 patients were evaluated by this division and a database was compiled and analyzed. The distribution of the rheumatic conditions has been compared with the data from other East Asian countries. The non-Thai data included children with rheumatic diseases in Singapore from KK Woman's and Children's Hospital, Tan Tock Seng Hospital, and the National Skin Centre and Singapore General Hospital reported by See Y et al in 1998 (n=170). The data also included a nationwide surveillance study throughout Japan, collected from 1,290 hospitals which was reported by Fujikawa S and colleagues in 1997 (n=1,606). Data from several Western countries was included for comparison.

The prevalence figures for pediatric rheumatic diseases in Thailand and other Asian countries are tabulated in Table 1⁽¹⁻⁵⁾. The prevalence figure for JIA subtypes are in Table 2⁽⁶⁻¹¹⁾

TREATMENT OF PEDIATRIC RHEUMATIC DISEASES

During the two year period, medication usage has been documented by the author. Non-steroidal anti-inflammatory drugs (NSAIDs) were normally the mainstay and the first choice of therapy in the treatment of pediatric rheumatic disorders. In Thailand, the only liquid NSAID available is ibuprofen under a variety of brand names. Other commonly used NSAIDs in pediatric rheumatology available in Thailand are indomethacin and piroxicam. Tolmetin is not available in Thai hospitals. Among COX-2 inhibitors, celecoxib, rofecoxib, nimesulide and meloxicam are available in Thailand. However, they are very expensive, particularly compared with health benefits and incomes, and these considerations severely limit their use. Disease modifying antirheumatic drugs (DMARDs) such as methotrexate, sulfasalazine, hydroxychloroquine and leflunomide are also generally available. Immunosuppressive agents, such as azathioprine and cyclophosphamide, are commonly used and reasonably priced.

Management of SLE was dominated by the use of prednisone, cyclophosphamide, azathioprine, and hydroxychloroquine. Cyclosporine-A (CSA) and mycophenolate mofetil (MMF) were expensive treatments and not often used. The management of children with lupus nephritis relapse or other complications requiring MMF, CSA, or other remissive agents was difficult. Biologics have not been available in Thailand until recently; only etanercept was imported and is only available through a large private hospital for well-to-do patients.

DISCUSSION

The niche of the pediatric rheumatologist in Asian countries remains fragile. In Thailand before my arrival, the patients were spread among many pediatric subspecialists. Children with juvenile idiopathic arthritis (JIA) were evaluated and managed by pediatric cardiologists. As pediatric cardiologists had long treated children with acute rheumatic fever, they were thought to have more expertise in managing children with arthritis. Children suffering from systemic lupus erythematosus (SLE) or systemic vasculitides complicated by renal

disease were followed by pediatric nephrologists. SLE children who had mainly hematologic or vasculitic skin diseases were typically evaluated and managed by pediatric hematologists and dermatologists, respectively. Teaching of medical students and pediatric residents about pediatric rheumatic diseases in pediatric curriculums was minimal. The pediatric age limit for most Thai children's hospitals or departments of pediatrics remains 13 to 15 years of age. Most adolescents with a variety of rheumatic conditions are evaluated and treated by adult internists and rheumatologists.

From my experience, many of the pediatric department chairpersons of the major Thai academic centers are not necessarily convinced that a pediatric rheumatologist is needed as part of their subspecialty team. Most do not believe in the pediatric rheumatology niche, usually supporting the status quo that children with rheumatic diseases can be adequately managed by other subspecialists as described above. The need for teaching in this area of pediatrics is often overlooked. Much remains to be done to develop pediatric rheumatology in Thailand and other Asian countries.

As expected, from our data, like in other Asian countries, SLE is more common than the western countries. Children with SLE in Thailand have more frequent vasculitic skin manifestation than in the West. JIA and systemic vasculitides, each contributes about a third of all pediatric rheumatic diseases seen. The majority children with systemic vasculitis in Thailand have Henoch-Schonlein purpura.

In regard to JIA in Thailand specifically, the systemic onset (SoJIA) subtype was the most prominent JIA, as it comprises about a half of all JIA cases in this single referral center. This was similar to the data reported in the Japanese study⁶. The reported frequency of SoJIA in Thailand, Japan, India and Kuwait, but not Taiwan, was at least double the frequency of cases in the Western countries observed (Table 2)⁶⁻¹¹. Polyarticular type JIA contributed only 8% of total JIA cases. Moreover, the majority of polyarthritis cases seen were the polyarticular course of SoJIA cases. Of the children with SoJIA, 48% had a

polyarticular course, which was higher than the West. We also saw less frequent rash (around 40%).

Using the ACR classification, patients with oligoarticular type contributed only a third of all JRA cases seen in the Asian countries compared to a half encountered in the Western countries. However, 15% of these patients had enthesitis-related JIA and 7% pursued polyarticular course or were reclassified as extended oligoarthritis according to the ILAR classification. Juvenile psoriatic arthritis was very rare in Thailand. Another interesting observation was that chronic uveitis as a complication of JIA was also very rare as the pediatric department at Siriraj Hospital had no cases. This absence of uveitis was confirmed by the pediatric ophthalmologists at the same institute. This may be partly attributed to the relative scarcity of oligoarticular and polyarticular JIA patients.

Management of pediatric rheumatic diseases in Thailand lags behind the US by about 5 years. Patients often have to pay for their medications and some drugs are just too expensive. Given financial concerns, expensive biologics and experimental treatments such as bone marrow transplantation are usually not an option in the Asian countries for children with recalcitrant and resistant, or immunosuppressive-dependent disease. Even if availability of these treatments is enhanced in the future, cost may make long courses of these therapies unrealistic.

In summary, in the experience of this author, pediatric rheumatologic conditions are not uncommon in Thailand and certainly not rare. It is probable that SLE and systemic vasculitides have a higher prevalence in this country, as well as in the neighboring Southeast Asian countries, than in the West. This difference is particularly striking in countries that share an East Asian ethnic origin. JIA constituted about a third of the pediatric rheumatology patients. However, the JIA subtype distribution was clearly different from the West, and varied among Asian countries. Thailand, as well as Japan, appeared to have more systemic JIA subtype (at least a half of total JIA cases) than other subtypes as compared to the Western countries. India had more prominent proportion of

polyarticular JIA. The options of therapies remain problematic due largely to patient income and each country's health budget. It is important that these therapy limits be kept in mind when drawing up treatment guidelines for pediatric rheumatic diseases.

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Table 1 Relative Frequencies of Rheumatic diseases in Pediatric Rheumatology Clinics, Asia and the selected Western Countries

Diseases	Thailand	Singapore	Japan	USA	UK	Can
Juvenile arthritis (%)		30	29	51	33	62
	50					
SLE (%)	30	52	29	7	1	4
Vasculitis (%)	27	NA	NA	10	2	3
Other* (%)	13	19 [†]	20 [†]	50	35	43

* Mechanical joint pain and other systemic autoimmune diseases.

† includes vasculitis

Ref: ¹⁻⁵

Table 2 Relative frequencies of Juvenile Rheumatoid Arthritis (JRA) subtypes.

JRA Subtypes	Thai* n=81	Japan	Taiw** n=228	S.India n=331	N.India n=361	Kuw*** n=108	USA ****
Systemic onset (%)	60	54	8	13	24	29	10
Polyarticular (%)	8	25	36	52	46	42	40
Pauciarticular (%)	32	21	56	35	30	29	50

Ref: ⁶⁻¹¹

*Thai=Thailand

**Taiw=Taiwan

***Kuw=Kuwait

****Cassidy Textbook