

Prevalence of pediatric systemic lupus erythematosus and juvenile chronic arthritis in a Chinese population: A nation-wide prospective population-based study in Taiwan

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Abstract

Objective

To estimate the national prevalence of systemic lupus erythematosus (SLE) and juvenile chronic arthritis (JCA) in Chinese children in Taiwan.

Methods

A nationwide prospective population based epidemiologic study for the prevalence of pediatric SLE and JCA was undertaken in Taiwan (23 million inhabitants). The population at risk was identified as children under the age of 16 living in Taiwan (5.78 million). All citizens have been obligated to participate in Taiwan's National Health Insurance program since 1995. This gave us access to nationwide case data from the Major Illness/Injury registry and enabled us to calculate population prevalence. The population data were derived from the 1999 Taiwan census.

Results

Three hundred sixty-five and 218 prevalent cases of pediatric SLE and JCA were identified, respectively. The prevalence of pediatric SLE was 6.3 per 100,000 (95% CI: 5.7–7.0). The prevalence in girls (11.2 per 100,000, 95% CI: 10.0–12.5) was 6.2 times higher than that in boys (1.8 per 100,000, 95% CI: 1.4–2.4). The prevalence of SLE substantially increased in children over the age of seven, especially in girls. The prevalence of JCA was 3.8 per 100,000 (95% CI: 3.3–4.3). The figures were similar for boys (3.5 per 100,000, 95% CI: 2.9–4.2) and girls (4.1 per 100,000, 95% CI: 3.3–4.9).

Conclusion

In this first population based epidemiologic survey of pediatric SLE and JCA in Taiwan, we provided a good starting point in our understanding of the epidemiology of these serious conditions in the Chinese population. The discrepancies between our prevalence figures and those reported from Western countries are possibly the results from true differences pertaining to ethnicity, geography or both. Future studies are necessary to elucidate the implications suggested by these data.

Key words

Systemic lupus erythematosus, juvenile chronic arthritis, prevalence, Chinese, children, epidemiology.

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Abbreviations:

SLE: systemic lupus erythematosus

JCA: juvenile chronic arthritis

MII: Major Illness/Injury

NHI: National Health Insurance

BNHI: Bureau of National Health Insurance

ICD-9-CM: International Classification of Diseases, 9th Revision, Clinical Modification

CI: confidence interval

Introduction

Although the epidemiology of rheumatic diseases has been investigated worldwide (1), reports for Chinese children are lacking. Systemic lupus erythematosus (SLE) and juvenile chronic arthritis (JCA) are two major rheumatic diseases of childhood, which often lead to serious morbidity and mortality. The prevalence of SLE in adults has been estimated to range between 12 and 50.8 per 100,000 in Caucasians (2-4), but little data in children are available. Similarly, a wide range can also be seen in the prevalence of JCA among different geographic locations: 0.83 to 400 per 100,000 children less than 16 years of age (5-8).

Epidemiologic studies of childhood rheumatic diseases are meaningful in the further development/evaluation of criteria for disease classification, description of the natural history and outcome in different disease entities, the identification of early prognostic factors, design of health care planning and, the identification of possible etiologic factors. Therefore, there has been considerable interest recently in the epidemiology of these two rare rheumatic diseases of children (9).

To date, there has been no study examining the prevalence of childhood rheumatic diseases in the Chinese population. We conducted a five-year prospective population based study to estimate the national prevalence of SLE and JCA in Chinese children aged less than 16 years in Taiwan.

Patients and methods

Study population

Taiwan is an Asia-Pacific country with the majority (> 95%) of inhabitants being ethnic Chinese. Covering an area of 45,981 km² and with a current population of 23 million, it has one of the highest population densities in the world. In Taiwan, all births, deaths, marriages, and divorces must be registered with the government's household registration bureaus. Information on education, employment and migration of all residents is also recorded. Household registration officers conduct home visits annually to ensure the accuracy of census data. Therefore, accurate cen-

sus information is available for epidemiologic research in Taiwan.

Prospective collection of cases through the Major Illness/Injury (MII) registry

The National Health Insurance (NHI) program, a government administered universal medical care insurance program, was launched March 1, 1995 in Taiwan. All citizens are required to enroll in NHI. As a result, health insurance coverage increased from 59% before NHI to the current universal coverage. NHI beneficiaries are required to co-pay a portion of medical costs to encourage the conscientious and efficient utilization of medical resources, thereby preventing waste and misuse. The primary function of the NHI co-payment system is to prevent indiscriminate use of medical resources. The Bureau of NHI (BNHI) simultaneously established a nationwide disease registry, namely the Major Illness/Injury (MII) registry, for keeping records on severe illnesses or injuries, such as malignancies, hemophilia, end-stage renal diseases, rheumatic diseases, major trauma, severe burns, etc. These patients are exempted from the co-payment obligation when they seek medical attention. A beneficiary with conditions officially qualifying as a major illness or injuries may apply to BNHI for the MII certificate by submitting a doctor's certificate of diagnosis and an application form.

The computerized information available for each patient within the MII registry includes basic demographic data, disease codes (International Classification of Diseases, 9th revision, Clinical Modification, ICD-9-CM), full diagnoses of diseases, date of registration and current status (alive or dead). Without renewal, the certificate will expire in 3.5 years. The database of MII registry is available for academic research. This specific population based disease registry allowed us to access nationwide case data on pediatric SLE and JCA and to calculate population prevalence. The study was performed prospectively from March 1, 1995 to December 31, 1999.

Disease definition

The disease code (ICD-9-CM) was

assigned by the doctor submitting the diagnosis certificate to the BNHI. Duplicate registration can be detected automatically by the computers of BNHI. Patients with SLE or JCA were identified through the MII registry according to the ICD-9-CM codes (710.0 for SLE and 714.0 for chronic inflammatory arthritis, respectively). Case verification was then performed by experienced pediatric rheumatologists through a detailed review of medical records. SLE was diagnosed according to the 1982 revised criteria for the classification of systemic lupus erythematosus (11), and JCA according to the 1977 European League Against Rheumatism (EULAR) diagnostic criteria (12).

Prevalence calculation

Prevalence figures were calculated using census data from the Taiwan Ministry of Interior, with the population at risk being classified as the number of children aged 0-15 years on December 31, 1999. Thus the point of prevalence measured on December 31, 1999. A prevalence case was defined as a child less than 16 years of age living in Taiwan on December 31, 1999, who met the diagnostic criteria for SLE or JCA, respectively.

Statistical analysis

The 95% confidence interval (CI) of the prevalence was calculated using the method provided by Schwertman and Martinez in order to make comparisons with other studies (13). A chi-square test was used to compare the proportion

of reporting hospitals between JCA and adult rheumatoid arthritis cases. SAS/win statistical software, version 6.12, was used for data analysis.

Results

The population of children at risk, 0 through 15 years of age, was 5,775,640 at the end of 1999. The distribution of sex among these children is as follows: male, 2,995,379; female, 2,780,261. Demographic statistics were obtained from the Taiwan Ministry of Interior, 1995 through 1999. Up to 1999, there were 387,331 MII certificate holders in Taiwan, 1.78% of the entire population. Of these MIIC holders, 9,658 patients (2.5%) had a diagnosis of SLE (ICD-9-CM, 710.0), and 373 of them (3.9%) were under the age of 16 on December 31, 1999; 231 patients (3.0%) with chronic inflammatory arthritis (ICD-9-CM, 714.0) were under the age of 16 at the end of 1999. After case verification, 365 and 218 cases who were less than 16 years of age at the end of 1999 fulfilled the diagnostic criteria for SLE and JCA, respectively.

Systemic lupus erythematosus

Three hundred sixty-five prevalent cases of pediatric SLE had been registered on December 31, 1999, giving a point prevalence of 6.3 per 100,000 (95% CI: 5.7—7.0). The prevalence in girls was 11.2 per 100,000 (95% CI: 10.0—12.5), and the prevalence in boys was 1.8 per 100,000 (95% CI: 1.4—2.4). The prevalence of SLE in girls was 6.2 times higher than that in

boys. The age-adjusted prevalence of pediatric SLE is shown in Figure 1. We found that the prevalence of SLE in girls substantially increased with age, from 0.65 per 100,000 at age one to 6.7 per 100,000 at age seven, and to 34.6 per 100,000 at age 15. The prevalence figure for boys slightly increased with age, from 0.0 per 100,000 at age one to 0.0 per 100,000 at age seven, and to 7.8 per 100,000 at age 15.

Juvenile chronic arthritis

For JCA, 218 prevalent cases were identified. The point prevalence of JCA was 3.8 per 100,000 (95% CI: 3.3—4.3). The prevalence of JCA was similar in boys (3.5 per 100,000, 95% CI: 2.9—4.2) and girls (4.1 per 100,000, 95% CI: 3.3—4.9). The age-adjusted prevalence of JCA is shown in Figure 2. The prevalence of JCA increased slightly with age both in boys and girls.

Discussion

We report the results of a five-year study, the largest population based epidemiologic study reported to date of childhood rheumatic diseases in the Chinese population in Taiwan. There have been numerous studies conducted to determine the frequencies of connective tissue diseases. Many investigations, however, have not been population based, and the numbers of patients on which the prevalence figures have been based are small (14). There are at least three benefits of population based registries for rare rheumatic diseases (14).

First, population-based registries allow researchers to monitor changing disease patterns in a country in relation to global trends. Without a registry, a rapid increase in occurrence of a disease might go unnoticed. Second, population based registries also allow geographic comparisons of disease incidence. Such comparisons have helped researchers define the relationship between the disease and potential environmental factors. Third, population based registries provide a collection of representative, rather than selected, cases for future investigations of etiologic or prognostic factors. In order to calculate prevalence, a well-defined

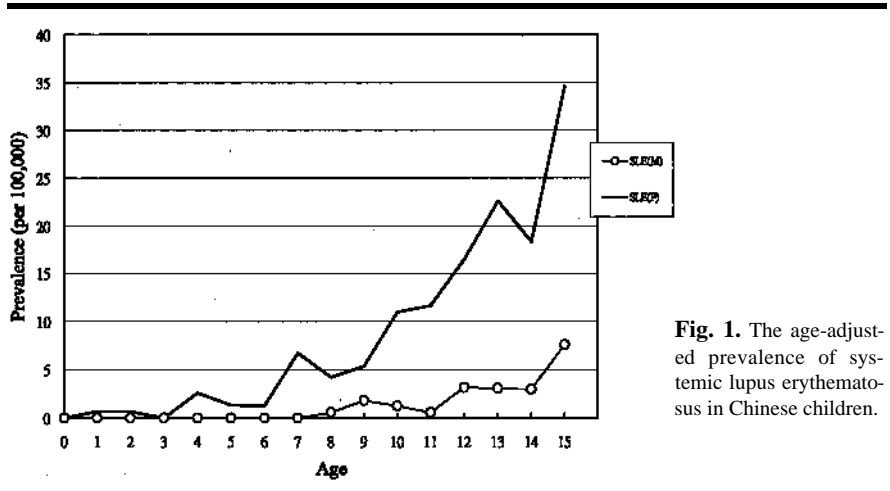


Fig. 1. The age-adjusted prevalence of systemic lupus erythematosus in Chinese children.

catchment population is a prerequisite for population based epidemiologic study (15).

However, in developing countries there may be difficulties in obtaining accurate census data, as discussed by Arguedas *et al.* (16). It is well known that census information is available and accurate for research in Taiwan. In addition, since NHI is a compulsory social insurance program for the entire population, the healthcare system in Taiwan has become more homogenous and socialized since 1995. Therefore, defining the study population has been much easier for research purposes. Furthermore, the establishment of the MII registry by the NHI program provides us with an opportunity to collect descriptive epidemiologic data on the nationwide population with rare rheumatic diseases, including pediatric SLE and JCA in Taiwan.

Our study revealed that the point prevalence of pediatric SLE was 6.3 per 100,000 for Chinese children less than 16 years of age, which was higher than that of the Finland population (1.5 per 100,000) (17). Our result confirms a higher prevalence of SLE in Chinese than in Caucasians in previous adult studies (18-20), pointing to a true difference that may pertain to ethnicity, geography or both. We also found that girls outnumbered boys in the prevalence of SLE (6.2: 1). This result corresponds with previously reported statistics in the United States (6.9: 1) (21) and in the United Kingdom (6.4: 1) (22). A predominance of adolescents, as in studies from Western countries, was noted in our survey, with the prevalence substantially increased in Chinese children over the age of seven.

Our study indicated that the prevalence of JCA in Chinese children was 3.8 per 100,000, which was much lower than previous studies of JCA or juvenile rheumatoid arthritis in Western countries (20 to 400 per 100,000) (7, 8, 15), with the exception of features from France (8 per 100,000) (6). Other findings include an almost equal prevalence of JCA in boys and girls.

The reasons for the extremely low prevalence of JCA in this study remain to be identified. A certain degree of under-

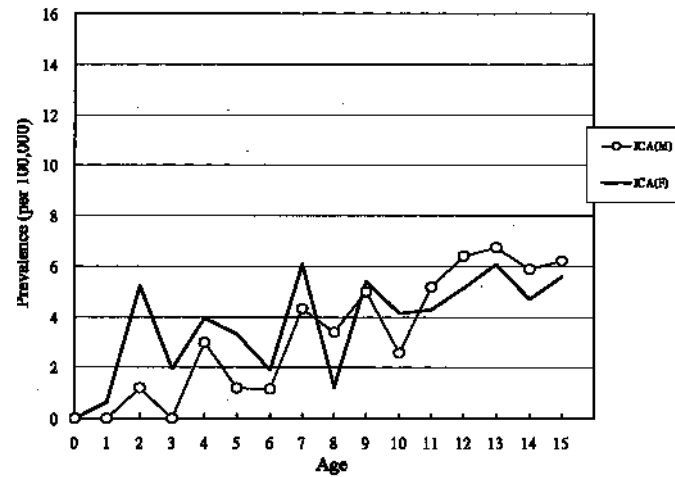


Fig. 2. The age-adjusted prevalence of juvenile chronic arthritis in Chinese children.

estimation may be an important contributing factor for this feature. First, underestimation may result from under-registration, because registration is voluntary, rather than obligatory. Given that registration relieves patients from co-payment obligations, we believed that the influence of under-registration would be mild. Second, one potential problem in the interpretation of these data is the possibility of under-diagnosis of JCA cases in Taiwan. It is unlikely that this is unique to Taiwan. A community-based study was conducted by Manners and Diepeveen in Australia, which demonstrated that most of the children with JCA had not previously come to medical attention (8). Their study showed significant lack of familiarity with childhood rheumatic complaints, both in the community and within the medical profession, with several parents seeking appropriate medical help for their child before the study, but with physicians failing to correctly diagnose the rheumatic problem (8). Petty's observation also revealed that many children with chronic arthritis are diagnosed as having chronic sprain or growing pains, often reflecting that many physicians still fail to recognize this disease (23).

Also of note in our study, if we compare the type of reporting hospitals for JCA and adult rheumatoid arthritis, 81% of cases with JCA were reported by tertiary medical centers, which was significantly higher than that of adult cases (61%, $P < 0.001$). This feature may imply that the low reporting rate

of JCA by general practitioners may result from under-recognition of JCA cases. It is therefore important in our next step to evaluate the awareness of childhood rheumatic diseases among general practitioners in Taiwan.

Third, another speculation could be that in the warmer climate of Taiwan milder cases have fewer symptoms, and patients are less likely to seek medical attention. Fourth, children who have gone into remission before 1995 would not be identifiable unless they had new symptoms during the study period. Therefore, the results of our analysis must be viewed in terms of the minimum prevalence, since only patients with active diseases were included. Although we note the limitations of this study, the results of this study present a good starting point in our understanding of the epidemiology of these serious conditions in Chinese children. Nonetheless, we must not ignore the possibility that ethnic or geographic differences, at least in part, contribute to discrepancies between our prevalence figures and those reported from Western countries. It is worthy noting that the prevalence of JCA in a Japanese population (0.83 per 100,000) (5) was also extremely lower than reported in Western samples (8 to 400 per 100,000) (6-8), even lower than that of our data (3.8 per 100,000). This may reflect a very low risk of arthritis developing in Asian populations. In support of this theory is the indication that the prevalence of rheumatoid arthritis in adults appears to be lower in Asian

populations than in Europe and North America (24, 25). In addition, our previous report (26), as well as other studies from Asian populations (27, 28), showed that the clinical features of Asian children with JCA were significantly different from Caucasian children by a relative male predominance, older age of onset, a lower ANA positivity rate, a lower chronic uveitis incidence and different subtypes of JCA. Furthermore, our previous study showed that HLA-DRB1*0405 is related to the development of polyarthritis and oligoarthritis in Taiwan, which is quite different from the results of Caucasian studies (29). This may indicate that there are true differences pertaining to genetic factors. Additionally, the panorama of infectious and other environmental triggers may also differ between Asian and Western countries. In summary, our preliminary observation reveals that the estimated prevalence of pediatric SLE (6.3/100,000) in the Chinese population of Taiwan is much higher than those reported in Caucasian populations, further confirming the higher prevalence of SLE in Chinese than in Caucasians in previous adult studies. The estimated minimum prevalence of JCA in Chinese children (3.8/100,000) is on the low end of the spectrum of previous studies. Combined with the report from Japan, the present report suggests a lower occurrence rate of JCA in Asian children than in Caucasians, possibly resulting from differences pertaining to ethnicity, geography or both. In this first population based epidemiologic survey of pediatric SLE and JCA in Taiwan, we have provided a good starting point in our understanding of the epidemiology of these serious conditions in the Chinese population.

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