Nationwide population-based epidemiologic study of rheumatoid arthritis in Taiwan

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Abstract

Objectives

Epidemiological studies of rheumatoid arthritis in Asia are rare. The aim of this research was to study the epidemiology and associated medical expenses of rheumatoid arthritis in Taiwan.

Methods

Cases of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria, were retrieved from the National Health Insurance Research Database with corresponding International Classification of Diseases, Ninth Revision code (ICD-9) 714.0 from January 2000 to December 2007, and limited to those 16 years and older. Age- and sex-specific incidences were estimated by dividing the incidence number by population data obtained from the Department of Statistics, Ministry of the Interior.

Results

There were a total of 40,995 cases. The average age-adjusted annual incidence rate was 15.8 per 100,000. The adjusted incidence rates were very stable at 20.9–25.2/100,000/year and 7.0–8.2/100,000/year for females and males, respectively, during the study period. The adjusted average incidence ratio of females/males was 3.1. The age-specific incidence peaked in the 60–64 and 70–74 year age groups for females and males, respectively. The adjusted prevalence rate increased steadily during the study period from 57.7/100,000 in 2000 to 99.6/100,000 in 2007. The average total yearly expense per patient increased from 1,155 United States Dollars (USD) in 2000 to 1,821 USD in 2007. Sicca syndrome (ICD-9 code 710.2) was the most common co-existing ICD-9 code.

Conclusion

This is the first incidence study based on the 1987 American College of Rheumatology criteria in Asia. The prevalence rate based on these criteria was lower than in previous Asia studies. The medical expenses increased continuously.

Key words

rheumatoid arthritis, prevalence, incidence, national health programmes, Taiwan

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Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease characterised by several distinctive patterns of progression after disease onset. Some RA patients have a mild form, but a progressive form results in bone and joint destruction if not treated properly (1). Since RA is also a systemic disease requiring long-term medication, there are many associated co-morbidities such as Sjögren's syndrome, cardiovascular disease, gastrointestinal disease, osteoporosis, and interstitial lung disease (2, 3). Therefore, RA will lead to high healthcare costs if not treated properly, and early treatment and good patient compliance will prevent joint damage, disability, and will reduce the occurrence of the above co-morbidities (4-6). There have been many epidemiological investigations on RA worldwide, especially in the West. RA is far more common in women than in men, with a female-to-male ratio of 3:1. The incidence of this disease increases with increasing age, and there is a decline in incidence in the elderly (*i.e.* those over 75 years) (7-9). Some environmental factors such as smoking, infection, and urbanisation also influence the occurrence of RA. In addition, there are geographic differences in disease prevalence. Northern Europe and North America have the highest prevalence, while the prevalence is lower in Asia and Africa (10). However, research in Asia is still relative scarce, with most epidemiologic studies having been conducted decades ago using older diagnostic criteria for RA (11).

The 1987 American College of Rheumatology (ACR) criteria are now the accepted criteria for RA diagnosis, having replaced the 1958 New York classification criteria. Some RA patients included in earlier studies may not fit the current definition of RA, therefore, it is difficult to compare previous epidemiological studies with recent studies based on the 1987 ACR criteria.

In a recent systemic review of the incidence and prevalence of RA based on the 1987 ACR criteria (12), North America and Northern Europe had higher prevalence rates ranging from 0.4% to 1%, compared with Southern Europe, ranging from 0.3% to 0.5%. The prevalence in Africa and Asia tends to be lower, with the majority of reports ranging between 0.2% to 0.3%. Incidence rates are also higher in North America and Northern Europe, ranging from 24 to 45 cases per 100,000 person-years. A lower incidence of 9 to 24 cases per 100,000 person-years has been reported in Southern Europe. However, the incidence of RA based on the 1987 ACR criteria has not been investigated in Asia. The aim of this study, therefore, was to conduct a nationwide analysis based on the 1987 ACR criteria to provide recent epidemiologic data in Taiwan.

Materials and methods

Data source

Taiwan launched the National Health Insurance (NHI) programme on March 1, 1995. Thereafter, the public has received comprehensive medical care. The coverage rate of the NHI was as high as 96.1% in 2000, increasing to 98.6% in 2007.

The National Health Insurance Research Database (NHIRD), a large digital database derived from this system by the Bureau of NHI and maintained by the National Health Research Institutes, is provided to medical specialists and university faculties in Taiwan for research purposes. Data in the NHIRD that could be used to recognise patients, physicians, pharmacists and medical institutions are encrypted before being sent to the National Health Research Institutes for database construction. Data are further scrambled before being released to each researcher. Therefore, information that could identify individuals at any level cannot be obtained from the database. Institutional Review Board approval was waived for this study.

Study subjects

Nationwide population-based data were obtained by using the annual outpatient claims and hospitalisation discharge claims from 2000 to 2007 from the NHIRD. The cases of RA were retrieved according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 714.0, and limited to those

Table I. Incidence and prevalence of rheumatoid arthritis in Taiwan.

	Total population ≥16 years old (millions)			New cases			Total cases			Crude rate							Adjusted rate						
										Incidence rate per 10^5/year			Prevalence per 10^5			F/M of incidence	Incidence rate per 10^5/year			Prevalence per 10^5			F/M of incidence
	F	M	T	F	M	T	F	M	T	F	M	T	F	M	T		F	M	T	F	M	T	
2000	8.5	8.8	17.2				10524	2558	13098				124.3	29.2	76					93.6	22.5	57.7	
2001	8.6	8.9	17.4	2932	908	3866	11890	2836	14763	34.1	10.3	22.2	138.5	32	84.6	3.3	25.2	7.7	16.5	102.6	24.4	63.3	3.3
2002	8.7	8.9	17.6	2956	879	3864	13643	3198	16896	34	9.8	21.9	157.1	35.8	95.9	3.5	24.8	7.4	16.2	114.4	27.0	70.7	3.3
2003	8.8	9	17.8	2980	894	3910	15405	3646	19125	33.9	9.9	22	175.4	40.5	107.6	3.4	24.3	7.2	15.8	125.5	30.1	78.0	3.4
2004	8.9	9.1	18	2935	947	3978	17108	4109	21350	33	10.4	22.1	192.2	45.2	118.7	3.2	23.2	7.5	15.7	135.3	32.9	84.7	3.1
2005	9	9.2	18.2	3204	1056	4260	18949	4602	23551	35.6	11.5	23.4	210.3	50.2	129.6	3.1	24.7	8.2	16.5	145.7	36.1	91.2	3.0
2006	9.1	9.3	18.4	3161	1067	4228	20699	5039	25738	34.6	11.5	23	226.2	54.4	139.8	3	23.6	8.2	15.9	154.1	38.7	96.8	2.9
2007	9.3	9.3	18.6	2860	931	3791	21937	5246	27183	30.9	10	20.4	236.7	56.2	146.1	3.1	20.9	7.0	14.0	158.5	39.5	99.6	3.0

F: female; M: male; T: total. There were 203 cases of missing or unknown gender data (16 in 2000, 26 in 2001, 29 in 2002, 36 in 2003, 96 in 2004, and none in 2005–2007). Adjusted rates are according to the age structure of the World Health Organisation World Standard Population.

aged 16 years and older. The data of the hospitalisation discharge claims include an encrypted personal identification number, date of birth, date of admission and discharge, relevant department, expenses, and first five ICD-9 codes. Outpatient claims files include an encrypted personal identification number, date of birth, date of service, department, expenses, and first three ICD-9 codes.

RA is included in the list of catastrophic illnesses which is published by the Department of Health, Executive Yuan, Taiwan. According to NHI regulations, the approval of the status of catastrophic illness for RA requires clinical and laboratory findings fulfilling the 1987 ACR criteria. Those who have a certificate of catastrophic illness are eligible for exemption from insurance premiums and co-payments. Therefore, data of RA with a certificate of catastrophic illness are accurate and reliable. All data in this study were verified with the catastrophic illness certificates provided in the NHIRD.

Statistical analysis

Figure drawing and statistics were carried out using SPSS version 15.0 for Windows (SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel 2007.

Incidence rates were calculated by dividing the numbers of new cases by population as published by the Ministry of Internal Affairs, Executive Yuan, Taiwan. Prevalence was calculated by dividing the number of total cases by population of the corresponding year. Average age- and sex-specific incidence rates were calculated by dividing the number of new cases in each age and sex group by the age- and sex-specific population, followed by averaging these data from 2001 to 2007. Age-specific population data for Taiwan were obtained from the website of the Ministry of the Interior, Executive Yuan, Taiwan (http://www.moi.gov.tw/stat/english/year.asp). The data on the website are the official population data of Taiwan. Age-adjusted incidence and prevalence rates were calculated according to age structure of the World Health Organisation (WHO) World Standard Population (http://www.who.int/whosis/indicators/compendium/2008/1mst/en/index.html). We defined new cases in the corresponding year as cases appearing in that year without appearing in previous years. The medical expenses were calculated from all inpatient and outpatient services if they had ICD-9-CM code 714.0 with a certificate of catastrophic illness. The average expense per service was calculated by the sum of the expenses divided by the number of services for inpatients and outpatients, respectively. The average length of stay was calculated by the sum of hospitalisation days in an acute ward divided by the number of inpatient services for all causes relating to the catastrophic illness. The medical expenses contained catastrophic illness related direct medical costs only. Direct medical costs not paid by the NHI, such as a single room, were not included. All indirect costs, such as time lost from work, disability, etc., were not included. The medical expenses were converted from new Taiwan Dollars (TWD) to United States Dollars (USD) using an exchange rate of 1 USD to 30 TWD.

Categorical data were analysed with the chi-square test, and comparisons of continuous data from the two groups were done with the independent *t*-test. *p*-values of less than 0.05 from two-sided tests were considered statistically significant.

Results

Table I shows the detailed sex-specific annual incidence and prevalence during the study period.

In total, 40,995 cases (new cases from 2001 to 2007 plus the total number of cases in 2000) were retrieved, containing 31,552 females, 9,240 males and 203 cases of missing or unknown gender data. The average female to male incidence ratio during 2001 to 2007 was 3.2. After adjusting according to the age structure of the WHO World Standard Population, the adjusted female to male incidence ratio was 3.1. The annual incidence rate ranged from 30.9 to 35.6 and 9.8 to 11.5 per 100,000 for females and males, respectively, and the adjusted incidence rate range from 20.9 to 25.2 and 7.0 to 8.2 per 100,000 for female and males, respectively. The overall annual incidence rate during 2001 to 2007 was 22.1 per 100,000, and the overall adjusted incidence rate was 15.8 per 100,000. The prevalence increased steadily from 76.0/100,000 in 2000 to 146.1/100,000 in 2007, and the adjusted prevalence also stead-

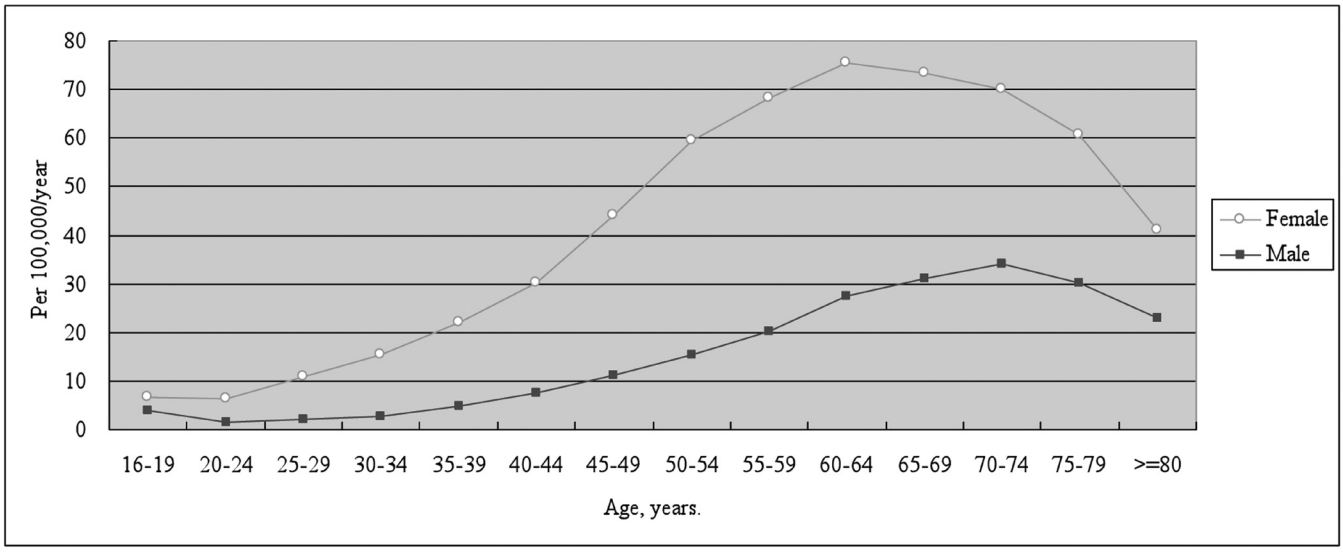

Fig. 1. Age-specific incidence of rheumatoid arthritis in Taiwan.

ily increased from 57.7/100,000 to 99.6/100,000. The incidence rates were very stable at 20.4–23.4/100,000/year and the adjusted incidence rates were 14.0–16.5/100,000.

Figure 1 shows the average age-specific incidences from 2001 to 2007.

The age-specific incidence increased with age after 20 years, peaked in the 60–64 and 70–74 year age groups for females and males, respectively, and then declined. A significantly higher age-specific incidence was observed in females compared to males in all age groups.

The 40,995 patients utilised 1,857,215 outpatient services and 27,749 inpatient services. On average, each patient utilised 11.5 outpatient services and 0.17 hospitalisations per year. The average length of stay in an acute ward was 10.2 days. The average expense was 102 USD for each outpatient service and 2,094 USD for each hospitalisation. The detailed annual expenses and numbers of outpatient visits and hospitalisations are listed in Table II.

The most common co-existing ICD-9 codes are shown in Table III. Sicca syndrome, a highly prevalent autoimmune disease, was the most common coexisting ICD-9 code. Other common coexisting codes were degenerative musculoskeletal disease (ICD-9 733.00, 715.90, 729.0), hypertension (ICD-9 401.9), diabetes mellitus type II (ICD-9 250.00), and gastric disease (ICD-9 533.90 and 536.9).

Among the 13,098 patients appearing in 2000, 70% of the female and 53% of the male patients were continuously followed up until 2007.

Discussion

This study is the first nationwide population-based study in Asia on the incidence and prevalence of RA for all age groups aged 16 years and over based on the 1987 ACR criteria. The diagnosis was based on ICD-9 coding in the present study, which may raise the question of diagnostic accuracy. However, given the medical environment in Taiwan, we believe the diagnosis of RA was reliable in most cases. First, basic chemical examinations, such as rheumatoid factor, and radiological examinations are available in most hospitals in Taiwan and routinely performed for the diagnosis of RA. Second, patients suspected to have autoimmune diseases are usually referred to rheumatologists for further confirmation. The patients can also directly visit rheumatologic clinics in medical centres for diagnosis and treatment without referral. Third, the application for a catastrophic illness certificate for RA requires thorough clinical and laboratory evaluations with results fulfilling the 1987 ACR criteria, and all data in this study were limited and linked to catastrophic illness certificates.

There have been incidence studies in Asia. A previous study in Japan reported an RA incidence rate of 9 to 35 per 100,000/year, but this study was performed decades ago and was based

Table II. Medical expenses due to rheumatoid arthritis in Taiwan.

Year	Patient number	Number of outpatient services	Sum of outpatient expenses USD	Average expense per outpatient service USD	Number of inpatient services	Sum of inpatient expenses USD	Average expenses per inpatient service USD	Average of total yearly expenses per patient USD
2000	13,098	133,152	10,877,831	82	2,232	4,255,543	1,907	1,155
2001	14,763	155,618	12,273,428	79	2,675	4,976,690	1,860	1,168
2002	16,896	185,303	15,423,855	83	3,213	6,630,970	2,064	1,305
2003	19,125	206,738	17,948,225	87	3,408	7,027,640	2,062	1,306
2004	21,350	252,262	25,748,642	102	3,882	8,468,654	2,182	1,603
2005	23,551	280,986	30,523,334	109	3,848	8,165,301	2,122	1,643
2006	25,738	312,308	36,091,714	116	4,234	9,197,536	2,172	1,760
2007	27,183	330,848	40,125,237	121	4,257	9,381,831	2,204	1,821

USD: United States Dollar.

Table III. Most common co-existing ICD-9 codes.

ICD-9	Disease	Number
710.2	Sicca syndrome	203,456
733.00	Osteoporosis, unspecified	173,217
401.9	Unspecified essential hypertension	146,279
533.90	Peptic ulcer, unspecified	61,637
715.90	Osteoarthrosis, unspecified	59,916
250.00	Diabetes mellitus without mention of complication	51,692
536.9	Unspecified functional disorder of stomach	47,747
465.9	Upper respiratory infection (acute)	36,954
729.0	Rheumatism, unspecified and fibrositis	36,225
710.0	Systemic lupus erythematosus	35,757

on previous identification criteria (13). The incidence in North America and Northern Europe has been reported to be around 20 to 50 per 100,000, with a lower incidence of 9 to 24 per 100,000 in Southern Europe based on the 1987 ACR criteria. However, previously there was not any incidence data reported in Asia based on the ACR 1987 criteria (9). Our study is the first in Asia to reveal an adjusted average annual incidence rate of 15.8 per 100,000, and an adjusted average female to male incidence ratio of 3.1 based on the 1987 ACR criteria.

In most populations, the incidence of RA increases with age until the eighth decade when it starts to decline. According to previous studies, the sex-specific rates peaked at a younger age group in women (60 to 70 years) compared to men (70 to 80 years) (6-8). Our data showed the sex-specific rates peaked at 60 to 64 years in women and 70 to 74 years in men, which is compatible with previous studies.

Our study showed an increasing prevalence with calendar year. Whether the increase in the prevalence of RA was real or due to the effect of health policies needs further investigation. Since RA is a disease with a long clinical course, many pre-existing patients would be enrolled steadily in the first few years after the establishment of the NHI program. This may have caused an underestimation of the prevalence in the first few years of the study, and the latest data in 2007 may therefore be less influenced by health policies and more reasonable. However, our data still showed a lower prevalence (0.10%) compared with two earlier studies in China, which also diagnosed RA on the basis of the 1987 ACR criteria. The first was published in 1993 and performed in Hong Kong, and reported a prevalence rate of 0.35% (95% CI 0.24–0.49%) (14). The second was performed in Shanghai from 1997 to 1998 and reported a prevalence rate of 0.28% (95% CI 0.15–0.41%) (15). There are some possible explanations for the higher prevalence rates in these studies. First, their studies were conducted in urban areas where environmental factors could be associated with higher prevalence. Second, these two studies were completed several years ago, and there has been a decline in the incidence and prevalence of RA in recent decades (13, 16-17). Third, these studies used active surveillance by interviews, however our study used claims data which did not include patients that did not seek medical care. Because there are different patterns of progression after RA onset (1), patients with a mild form may not seek medical care during the quiescent period. In addition, many RA patients have poor compliance. One study showed that only 77% of patients took medications for RA throughout a 3-year observation period (18). Our data showed similar results, in which 70% of the female and 53% of the male patients appearing in 2000 were continuously followed up to 2007. These patients are prevalent RA patients, however, they were not included in our population identified from claims data due to loss of follow-up. These reasons may explain the lower prevalence rate in our study. In addition, the cause of the lower prevalence rate but comparable incidence rate may be explained by the fact that the loss to follow-up cases who did not seek medical resources after a certain point of clinical course, due to mild disease activity or poor compliance, cannot be detected by claims data.

Our study showed that common co-existing ICD-9 codes were Sicca syndrome, metabolic syndrome (diabetes, hypertension), gastric disease, and musculoskeletal disease (osteoporosis, osteoarthritis, and rheumatism). These co-morbidities are commonly present in RA, as reported in previous studies (2, 19, 20).

Compared with our previous study on SLE using the same methodology, the average expense per outpatient service was higher in RA than in SLE (21). Possible explanations include that more kinds of expensive immunomodulators, such as cyclosporine, are reimbursed for RA but not for SLE in Taiwan, more COX-II inhibitors are prescribed in RA, and biologic agents (such as tumour necrosis factor antagonist, anti-CD20 agent) for RA have been launched in recent years.

However, there are limitations to this study which have to be addressed. The age of disease onset was not available in the database. Catastrophic illness status will not be approved until firm evidence has been obtained. Therefore, the annual incidence of RA in this study represents the yearly number of new catastrophic illness approvals for RA, and the prevalence of RA represents the yearly number of total RA cases with approval of catastrophic illness status with clinic visits. The age of age-specific incidence in the present study represents the age of approval of catastrophic illness, and the age of approved catastrophic illness is certain to be older than that of symptom onset.

In conclusion, this is the first epidemiological study on the incidence of RA based on the 1987 ACR criteria in Asia. The prevalence rate based on these criteria was lower than in previous Asia studies, and the medical expenses increased continuously.

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