

科技部補助
大專學生研究計畫研究成果報告

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| 計 畫 名 稱 | ： 台灣僵直性脊椎炎(Ankylosing spondylitis)的流行病 學研究：2000年到2013年 |
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一、中、英文摘要及關鍵詞 (keywords)

1. 中文摘要

研究目的：分析 2001 年至 2013 年台灣僵直性脊椎炎的流行病學，包含盛行率及發生率等。

研究方法：使用健保資料庫進行資料分析，分析軟體為 SAS。僵直性脊椎炎的診斷採用 ICD-9 的診斷碼，並且需在一年之中的 180 天內有三次以上的門診或是一次住院。盛行率以及發生率依據 2000 年的人口為基準進行年齡標準化。

結果：2000 年至 2013 年間，盛行率由 0.077% 成長至 0.127%，每年成長了 4%。發生率則是由 2001 年間的 41.51(95% CI: 37.01-46.02) /10⁵ 人年降到 26.41(95% CI: 22.84-29.98) /10⁵ 人年。

結論：在 2000 至 2013 年間，盛行率呈現穩定成長了 1.64 倍，而發生率逐年下降。雖然女性的發生率較男性低，但是所占比率有上升趨勢。

2. Abstract

Aim:

To investigate the epidemiological trends of ankylosing spondylitis in Taiwan from 2000 to 2013.

Methods:

The data were sourced from the National Health Insurance Research Database (NHIRD). The 2000-2013 claim records were collected, excluding persons under 16 years old in 2000. Diagnosis of ankylosing spondylitis mentioned in this study was retrieved by the International Classification of Diseases-9 code. Ankylosing spondylitis patients were defined as those with at least three outpatient visits or one admission within 180 days in one calendar year. Age-standardized annual prevalence and incidence were estimated according to the reference population in 2000, with the sex proportion analyzed. All statistical analyses were conducted using the SAS statistical package.

Results:

The age-standardized prevalence increased by 4 % annually from 0.077% in 2000 to 0.127% in 2013, while the incidence decreased from 41.51(95% CI: 37.01-46.02) in 2001 to 26.41(95% CI: 22.84-29.98) per 10⁵ person-years in 2013. Men had higher

prevalence and incidence, and the male/female incidence ratio decreased from 2.23 in 2001 to 1.52 in 2013.

Conclusion:

From 2000 to 2013, the prevalence of AS has increased of 1.64 times to 0.127%, while incidence decreased by 4% annually. The female proportion in the new case was increasing, which may raise awareness of the diagnosis of female in AS and health-care planning.

Keywords: 僵直性脊椎炎、盛行率、發生率、ankylosing spondylitis, prevalence, incidence, epidemiology

二、簡介

Ankylosing spondylitis (AS), a major subtype of spondyloarthritis, is a chronic inflammatory disease which primarily affects patients' spine and sacroiliac joints. Clinical presentation commonly include lower back pain, reduced spinal mobility, sacroilitis, and extra-axial features such as peripheral arthritis. As the disease progresses, continuous inflammation may eventually lead to loss of spinal mobility, affecting social and occupational performances [1, 2]. Male sex and HLA-B27 positive population are considered risk factors for the disease [3].

The epidemiology of ankylosing spondylitis has been studied worldwide with various results due to different study designs and geographic factors. Most studies were based on hospital records or questionnaire survey, while studies using public health database are relatively rare. A systematic literature review in 2014 estimated that prevalence rate in Europe (0.238%) and North America(0.319%)is higher than that of Asia(0.167%) [4]. With the progress of technology and medical treatment, the epidemiological trends between male and female are on the change. In Canada, a population-based study showed a decreasing trend of male/female prevalence ratio from 1995 to 2010, and the female incidence rate rising significantly[5].

Previous epidemiological studies were mostly based on hospital records or questionnaire survey, while large-scale studies using public health database are relatively rare. In 1994, a study based on three administrative areas in Taiwan showed that the prevalence of ankylosing spondylitis was 0.54% in rural area, 0.19% in subrural area and 0.4% in urban area[6].

The change in prevalence and incidence of AS comes to be of especial importance due to improving technology and diagnosis methods. With recent improved understanding of pathogenesis[7], a better understanding of the epidemiology of AS in Taiwan would allow for more efficient application of new treatment strategies for the improvement of healthcare quality and quality of life in the affected population.

In this study, we aim to estimate the incidence and prevalence of ankylosing spondylitis from 2000 to 2013 using population-based data extracted from the Taiwan National Health Insurance Research Database (NHIRD).

三、研究方法

Database

Taiwan National Health Insurance (NHI) is a government-run, uni-payer health program launched in 1995[8]. Aiming to provide socially affordable and universal health care for citizens, the NHI coverage rate was 99.8% in 2018[9]. The NHI research database (NHIRD) is composed of data from the enrollment and provider files. All data were encrypted to confirm anonymity before being submitted to the NHRI, and data that may result in identifications of individuals were excluded before released to researchers[10]. The Bureau of NHI routinely exerts random reviews of patient charts to ensure coding validity. These computerized databases facilitate population-based studies on health care related topics.

Approved by the Ethics Review Board of Chung Shan Medical University (CS15134), this study used the 2000 Longitudinal Health Insurance Research Database (2000 LHIRD) that involved 1 million beneficiaries randomly sampled from registration files in 2000. We collected the 2000-2013 claim records, included outpatient visit, admission, from 2000 LHIRD.

Study population

The study population was identified from registry files for beneficiaries from 2000 to 2013, and the demographical variables including age, sex was selected. The distribution of age group in 2000 was defined as the standard population and used for calculation of standardized prevalence or incidence rate. Persons aged <16 years old in 2000 were excluded from population. When we analyzed the annual incidence rate, we removed the prevalent cases from population (denominator).

The 2000-2013 annual prevalent or new AS cases were identified by ICD-9-CM code 720.0, and the diagnosis had at least three outpatient visits or one admission within 180 days in one calendar year. In order to improve the validity of the new AS cases, we identified the new AS cases since 2001.

Statistical Analyses

All statistical analyses were conducted using the SAS statistical package (Version 9.4; SAS Institute, Inc., Cary, NC). The Poisson regression was applied to analyze linear trend of rates.

四、研究結果

Trends of Prevalence and Incidence of AS from 2000 to 2013

The annual trend of prevalence and incidence of AS from 2000 to 2013 is shown in Figure 1. The age-standardized prevalence rate in patients increased significantly from 77.61(95% CI:71.43-83.78) in 2000 to 127.70 (95% CI: 119.80-135.60)per 100,000 persons in 2013. The age-standardized incidence rate, on the other hand, decreased from 41.51 (95% CI: 37.01-46.02) in 2001 to 26.41(95% CI: 22.84-29.98) per 100,000 person-years in 2013(Table 1). The prevalence rate showed an annual increase of 4% ($p<0.001$), and the incidence rate showed an annual decrease of 4% ($p<0.001$) respectively.

Gender Differences in Prevalence and Incidence Rates

The annual increment of prevalence was 5% and 3% for males and females respectively, while the annual decrement of incidence was 5% and 3% respectively (Figure 2).

The sex ratio of prevalent rate and incident rate from 2001 to 2013 was then calculated. Male/female ratio of prevalent rate was relatively stable, with 2.51 in 2001, 2.63 in 2007 and 2.37 in 2013(figure 3a). On the other hand, though men have higher incident rate than female, the male/female ratio of incidence showed an overall decreasing trend, from 2.23 in 2001to 1.52 in 2013(figure 3b).

五、結果討論

This is a population-based study using the NHIRD database. The results showed that from 2000 to 2013, prevalence of AS increased from 77.61/100,000 to 127.7/100,000. The incidence, on the other hand, showed decreased trends from 41.51/100,000 person-years to 26.41/100,000 person-years, with decreasing male/female ratio.

The global prevalence of AS is reported varying across demographics, along with the geographic distribution profile of HLA-B27. Compared to the European countries, the prevalence of HLA-B27 gene in Taiwan is relatively low [11-15]. A systematic literature review by Dean et al found the mean AS prevalence in Asia to be 0.167% and the mean weighted AS prevalence in Asia (when the difference in the size of the study sample was accounted for) to be 0.18%, lower than that of Europe and North America. [4] Previous study by Chou et al found that the average prevalence of AS

was around 0.19% to 0.54% in Taiwan[6]. The results of our study were found to be slightly lower, being about 0.1277%. However, the prevalence in Taiwan is higher than in Korea (0.05% in 2015) and Japan (6.5/100,000 persons) [16, 17]. Besides the prevalence of HLA-B27, different diagnostic methods and study designs may lead to diverse results between studies.

Epidemiological studies have observed the increasing prevalence trends of AS in different countries. Recent study in Korea utilized the country's Health Insurance Review Agency (HIRA) database and found that the country saw an annual linear increase in prevalence of AS cases from 0.03% in 2010 to 0.05% in 2015[17]. A study in Norway found that the prevalence of AS in 1990 was around twice of that in 1980[18]. Our own results also reflected a significant increase in prevalence from 2000 to 2013. Though incidence showed decreasing trends, longer life expectancy, early diagnosis, updated treatment, decreased mortality rates and increased knowledge of rheumatic diseases may cause the increasing prevalence of AS.

In this study, the male/female ratio of the prevalence remained relatively steady, being around 2.37-2.74 from 2000 to 2013. Gender ratio of incidence, on the other hand, decreased from 2.23 in 2001 to 1.52 in 2013. Though men generally higher prevalence than women in AS, the male/female ratio is decreasing, being around 2-3:1 in recent studies [19-22]. Previous studies showed that the slow progression of clinical presentations and radiographic change in female patients may cause a longer delay in diagnosis compared to male patients[23]. Public awareness and the use of MRI may be the reason of the earlier detection of the disease, leading to increasing female population of AS [5, 24].

The strength of the study is that we utilized data from the NHID, which allowed us to analyze a reliable source of data, while avoiding selection bias. However, as severity of the disease, clinical status, lifestyle, and genetic factors could not be recorded in the NHI research database, further studies may be required to understand the influence of these variables on epidemiology. Also, patients who did not seek for medical help would not have medical records in the database, which leads to us possibly underestimating the AS population in Taiwan. Nonetheless, NHI covers and provides medical access to about 99% of the population in Taiwan[8]. Our results remain reliable to represent the epidemiological trends of AS.

六、結論

The prevalence of ankylosing spondylitis had significantly increased in Taiwan from 2000 to 2013, while the incidence decreased. The female proportion in the new case was increasing, which may raise awareness of the diagnosis of female in AS and health-care planning. Further studies investigating in the distribution of the genetic factors and other risk factors in the disease population is required to have a more profound understand of the ankylosing spondylitis population in Taiwan.

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八、附表與附圖

| Year | Population | Prevalent case | Prevalence rate ⁺ (95% C.I.) | New case | Incidence rate* (95% C.I.) |
|------|------------|----------------|---|----------|----------------------------|
| 2000 | 782166 | 607 | 77.61(71.43-83.78) | - | - |
| 2001 | 786095 | 646 | 82.25(75.91-88.60) | 326 | 41.51(37.01-46.02) |
| 2002 | 788665 | 713 | 90.34(83.70-96.98) | 316 | 39.82(35.42-44.22) |
| 2003 | 769328 | 722 | 93.63(86.77-100.50) | 301 | 38.45(34.08-42.82) |
| 2004 | 761175 | 732 | 95.85(88.85-102.90) | 304 | 39.74(35.23-44.24) |
| 2005 | 785193 | 759 | 96.44(89.51-103.40) | 262 | 32.86(28.83-36.88) |
| 2006 | 794016 | 814 | 102.70(95.54-109.80) | 267 | 33.45(29.38-37.51) |
| 2007 | 801074 | 802 | 101.00(93.87-108.00) | 226 | 28.29(24.53-32.04) |
| 2008 | 808501 | 840 | 104.30(97.07-111.40) | 215 | 26.47(22.86-30.08) |
| 2009 | 814615 | 884 | 109.30(101.90-116.70) | 190 | 23.98(20.49-27.47) |
| 2010 | 820896 | 967 | 118.20(110.60-125.90) | 231 | 28.15(24.41-31.89) |
| 2011 | 828046 | 1001 | 120.30(112.60-128.00) | 236 | 28.73(24.95-32.52) |
| 2012 | 835042 | 1086 | 129.40(121.50-137.40) | 249 | 29.68(25.86-33.50) |
| 2013 | 840193 | 1084 | 127.70(119.80-135.60) | 232 | 26.41(22.84-29.98) |

Table 1. Prevalence and incidence of ankylosing spondylitis in Taiwan from 2000-2013

⁺ per 100000 persons, standardized by 2000 standard population

* per 100000 person year, standardized by 2000 standard population

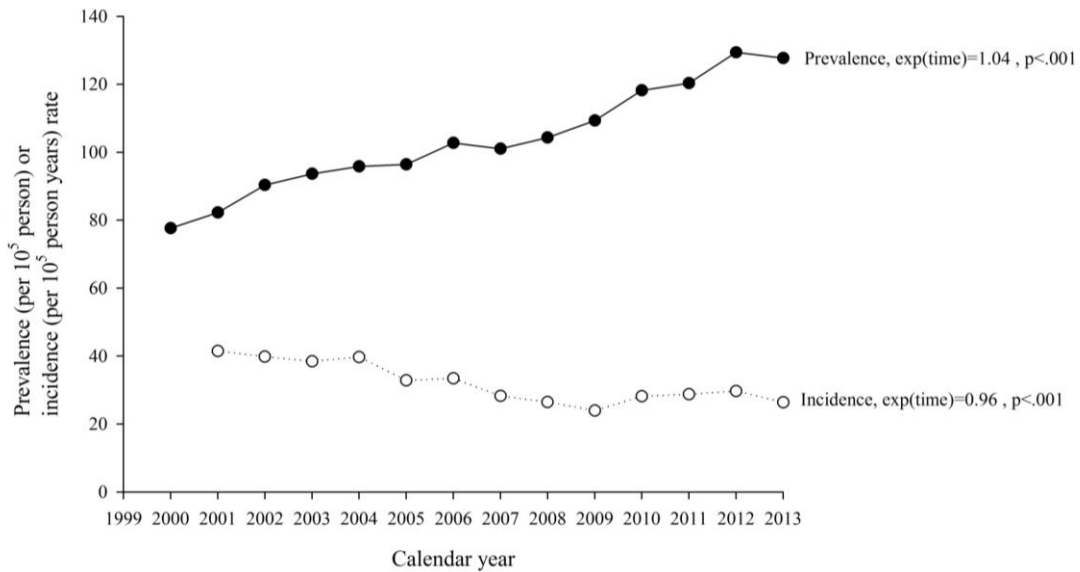


Figure 1. Age standardized prevalence (per 10⁵ persons) or incidence rate (per 10⁵ person-years) of ankylosing spondylitis

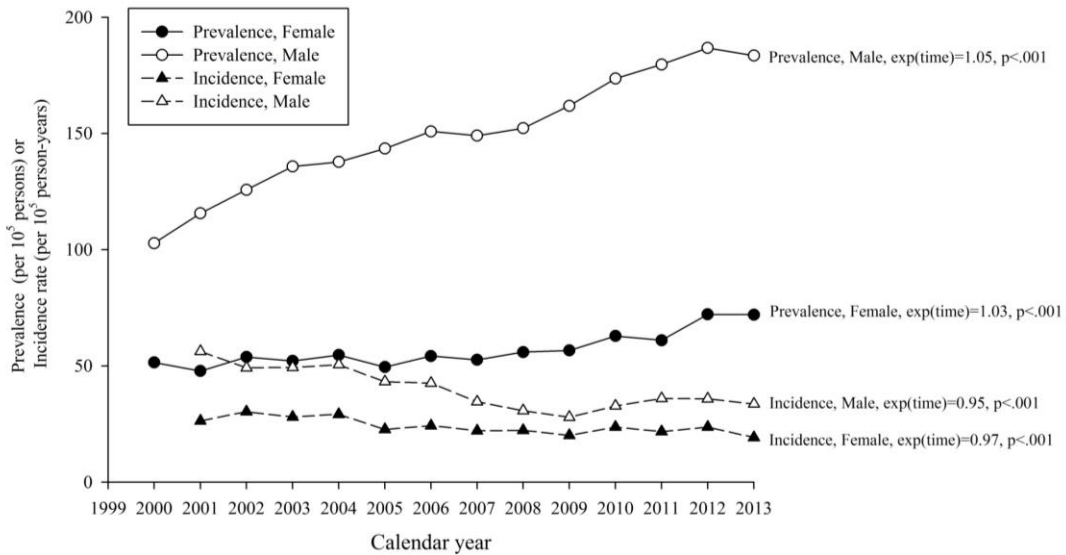


Figure 2. Age standardized prevalence (per 10⁵ persons) or incidence rate (per 10⁵ person-years) for ankylosing spondylitis stratified by sex.

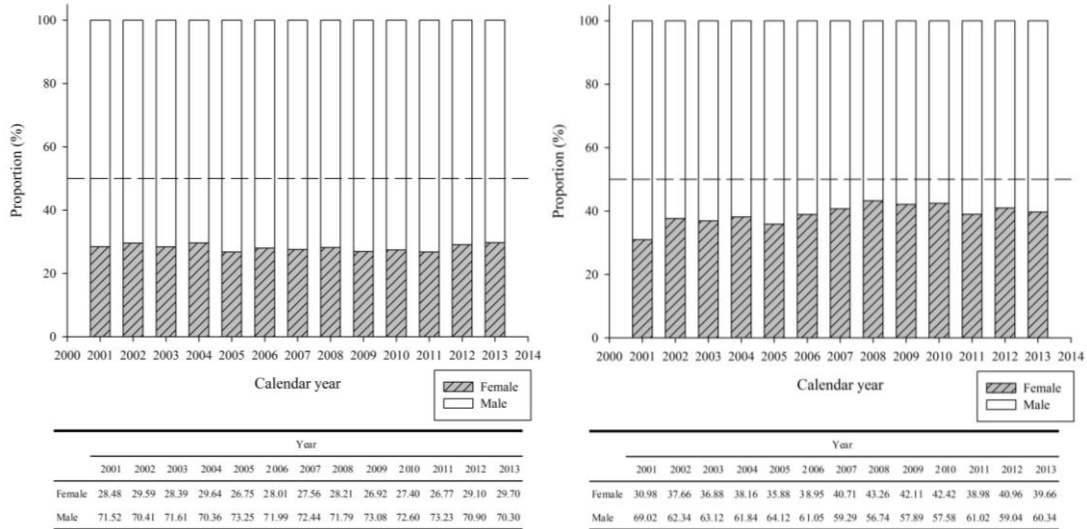


Figure 3. Sex proportion of annual ankylosing spondylitis (a) prevalent cases, and (b) new cases from 2001 to 2013

九、科技部補助專題研究計畫成果自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現（簡要敘述成果是否具有政策應用參考價值及具影響公共利益之重大發現）或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估

■達成目標

未達成目標（請說明，以 100 字為限）

實驗失敗

因故實驗中斷

其他原因

說明：依據資料分析得到的結果，目前初步完成論文，修飾後將投稿期刊。

2. 研究成果在學術期刊發表或申請專利等情形(請於其他欄註明專利及技轉之證號、合約、申請及洽談等詳細資訊)

論文：已發表 未發表之文稿 撰寫中 無

專利：已獲得 申請中 無

技轉：已技轉 洽談中 無

其他：(以 200 字為限)

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性，以 500 字為限）。

僵直性脊椎炎的患者由於對中軸骨骼有所影響，所以對於日常生活影響較大，針對疾病的流行病學的研究能夠讓大眾對於疾病的趨勢有更多了解，也能夠更加明白對於疾病的診斷、治療方向是否需要調整。此次研究中進分析了發生率、盛行率以及男性、女性的比例，因為僵直性脊椎炎的診斷通常在年輕男性居多，之後應能更進一步分析年齡分層，探討此疾病的在男性、女性不同年齡的分佈比率以及疾病發生年紀是否隨著時間而有所不同，提升對疾病的瞭解。

4. 主要發現

本研究具有政策應用參考價值：否 是，建議提供機關：衛生福利部

(勾選「是」者，請列舉建議可提供施政參考之業務主管機關)

本研究具影響公共利益之重大發現：否 是

說明：(以 150 字為限)

本研究描述台灣的僵直性脊椎炎在 2000 年至 2013 年之間的流行病學變化，可做為健康照護計畫、治療規劃的參考。未來還需更進一步的研究，將結果提升應用層面價值。