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Population-Based Big Data Analysis on Disease Patterns in Patients Identified With Juvenile Idiopathic Arthritis Using National Claims Data

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ABSTRACT

Background: This study aimed to identify epidemiologic data, including prevalence and incidence, of patients with juvenile idiopathic arthritis (JIA) in accordance with the diseases diagnostic code and Rare Intractable Disease Registration (RIDR) code from the claims data of the Health Insurance Review and Assessment Service (HIRA), the representative secondary data in Korea.
Methods: We conducted a retrospective analysis of the national claims data of the HIRA. The study population included 1,728 patients with JIA who 1) had records with diagnostic codes in the format prescribed by the International Classification of Diseases, 10th Revision M08 and the RIDR code V133 between January 1, 2010, and December 31, 2019, and 2) were aged < 16 years as per the definition of JIA. We categorized the patients by age at diagnosis, annual prevalence, and incidence per 100,000 individuals for the study period. Moreover, the study population was stratified by age and gender for subgroup analysis.
Results: The overall prevalence rate for the total, male, and female population was 15.9 (14.5–16.8), 15.4 (13.1–17.0), and 16.4 (15.9–16.9) per 100,000 individuals, respectively. Additionally, the overall incidence rate for the same populations was 2.2 (1.8–2.8), 2.3 (1.7–2.9), and 2.1 (1.8–2.6) per 100,000 individuals, respectively.
Conclusion: To the best of our knowledge, this is the first study presenting the epidemiologic data, including prevalence and incidence, of patients with JIA using population-based claims big data in Korea. The results of this study will aid in understanding the current status of JIA in Korea and Asia and in health care planning.

Keywords: Juvenile Idiopathic Arthritis; Incidence; National Claims Data; Prevalence

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common form of chronic arthritis occurring in children aged < 16 years. The cause of JIA is unknown, and symptoms can persist for ≥ 6 weeks. JIA can be categorized into various heterogeneous subgroups based on the criteria of

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Disclosure

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Author Contributions

Conceptualization: Lee SH, Ahn JG, Jeong DC. Data curation: Min EJ, Lee SH, Jo JY, Jeong DC. Formal analysis: Min EJ, Lee SH, Ahn JG, Jeong DC. Investigation: Min EJ, Jo JY, Ahn JG, Jeong DC. Methodology: Min EJ, Lee SH, Jo JY, Ahn JG, Jeong DC. Resources: Jo JY. Supervision: Ahn JG, Jeong DC. Visualization: Lee SH, Jo JY, Jeong DC. Writing - original draft: Min EJ, Lee SH, Jo JY, Ahn JG, Jeong DC. Writing - review & editing: Min EJ, Jo JY, Ahn JG, Jeong DC.

the International League of Association for Rheumatology (ILAR).[1,2] JIA can only be clinically diagnosed as no single blood test or imaging modality can definitively confirm the disease.[3] Although blood tests and imaging can support the diagnosis, they are primarily used for assessing prognosis and monitoring treatment response. Therefore, it is essential to exclude other conditions that may present with similar symptoms.[4] Differential diagnoses for JIA include neoplastic, infectious, and other rheumatologic conditions involving the joints.[5] JIA often manifests with various inflammatory signs in the joints, such as pain, swelling, warmth, and loss of function. In addition to these, JIA-related inflammation may lead to complications such as uveitis, skin rashes, fever, and growth abnormalities.[6] Hence, early and active treatment from the onset of symptoms is crucial to prevent disease-related complications in growing children, highlighting the importance of medication and comprehensive disease monitoring for effective disease management.[7,8] Several studies, particularly those conducted in Europe and the United States, have calculated the incidence rate and prevalence of JIA and reported clear differences among geographical regions and ethnic groups. Estimates from different studies and countries significantly vary.[9,10] The pooled incidence rate of JIA calculated in 2014 from 43 studies was approximately 1.6–23 in 100,000 individuals, whereas the pooled prevalence rate was approximately 3.8–400 in 100,000 individuals.[11]

Administrative health databases are useful for population-based health assessments as they can support large sample sizes, enable long-term tracking, and provide total population representation. Many epidemiological studies use these databases globally, with results continuously refined through validation. Such studies contribute to understanding disease trends, including incidence and prevalence rates, and to improving policies for disease control.[12-14] For example, in the United States, administrative data from a large insurance database has been used to study drug use trends in children with JIA.[15-17]

In Korea, the Health Insurance Review and Assessment (HIRA) database, which is a part of the National Health Insurance (NHI) system, can provide comprehensive national data on treatment, procedures, and prescriptions. The HIRA database has been widely used in epidemiological studies to assess disease prevalence, patient characteristics, and drug usage patterns.[18-20]

This study aimed to conduct a population-based epidemiological analysis of the disease characteristics, including incidence rate, prevalence rate, and other characteristics, of JIA using the HIRA database, an administrative database representing patients with JIA in Korea.

METHODS

Data source

This study analyzed claims data from the HIRA database between January 1, 2007, and December 31, 2019. HIRA is a government agency that oversees and evaluates healthcare insurance expenses of the entire population of Korea. These data contain detailed information, including patient diagnoses, treatments, procedures, surgical histories, and prescription drugs, across the range of health care settings, regardless of geographic location.

Definitions

The annual disease prevalence rate was calculated by dividing the number of patients by the total population eligible by age criteria for each group annually. The annual incidence

rate was calculated by dividing the number of new cases by the at-risk population for each group annually. The at-risk population was calculated by subtracting the number of patients diagnosed in the previous year from the census population for each age group. Overall prevalence and incidence rates were computed as the averages of the annual prevalence and incidence rates, respectively, for the study period (2010–2019).

The index date was defined as the first recorded diagnosis with the ICD-10 code as M08. To establish this date, a 3-year pre-index period (2007–2009) was used to verify the initial presence of the ICD-10 code M08 and the Rare Intractable Disease Registration (RIDR) system code for JIA, V133, confirming no prior diagnosis of JIA. In 2001, the Korean government initiated a national financial support program for patients with rare diseases, followed by the establishment of the RIDR system in 2009. Patients had to meet specific criteria set by the NHI system to be considered eligible for the RIDR program. For JIA, these criteria include laboratory and radiologic tests in accordance with established diagnostic or classification standards, along with physicians' clinical judgment. The disease duration was defined as the number of days from the index date to the date when the last prescription was exhausted or December 31, 2019, whichever was earlier.

Study population

The process of establishing the study population is summarized in **Fig. 1**. We extracted patients' records from the database, specifically those with ICD-10 codes M07 (psoriatic arthropathy), M08 (juvenile arthritis), and M09 (juvenile arthritis in psoriasis) and those aged ≤ 30 years, from January 1, 2007, to December 31, 2019 (n = 354,942).

As the first step, we excluded patients who were older than 19 years at the index date, selecting only those diagnosed with ICD-10 code M08 before age 18, resulting in a sample of 26,080 patients. This initial age limit was based on the common perception in Korea that adolescence extends up to 19 years of age. However, we further refined our study population to include only children aged ≤ 16 years to align with international ILAR standards for JIA, decreasing the cohort to 21,216 patients. Additionally, patients whose index date was after

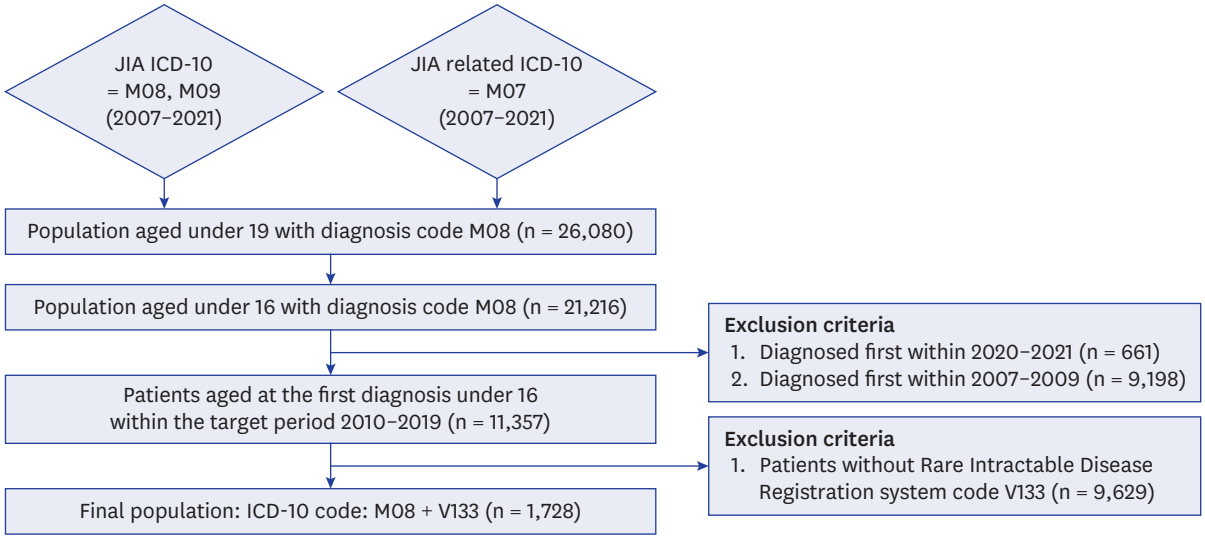

Fig. 1. Flow diagram of study population selection from the Health Insurance Review and Assessment Service database.
JIA = Juvenile Idiopathic Arthritis, ICD-10 = International Classification of Diseases 10th Revision.

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2020 or before 2010 were excluded, resulting in a cohort of 11,357 patients. To further refine the study population, patients without ICD-10 code M08 and RIDR code V133 were excluded, leaving a final cohort of 1,728 patients.

To facilitate further research, we divided the study population into four subgroups, toddler, < 4 years old; preschool age, 4–7 years old; school age, 7–13 years old; and adolescent, 13–16 years old.

Statistical analyses

The index date was used to estimate the incidence and prevalence rates of JIA. Patient demographics including gender and age were reported on the basis of the index date. Means, standard deviations, medians, and ranges (minimum and maximum) were estimated for continuous variables, and frequencies and proportions were calculated for categorical variables. Statistical analyses were performed using the SAS (version 9.3) software program (SAS Institute, Inc., Cary, NC, USA). Annual prevalence and cumulative incidence rates were calculated for each year, and all results were further stratified by age and gender. In all analyses results, *P* values < 0.05 are considered statistically significant.

Ethics statement

This study was approved by the Institutional Review Board (IRB) of the Catholic University (MC22ZSDI0014), St. Mary's Seoul Hospital (KC22ZSDI0051), and Yonsei University Severance Hospital (4-2021-1557). The requirement for obtaining consent to use the HIRA data was waived by the IRB as it involves the use of anonymized secondary data.

RESULTS

Demographics

The population demographics at index date are presented in **Table 1**. The number of patients with JIA at < 16 years of age was 1,728, with 54.1% (n = 934) males and 45.9% (n = 794) females. The age at diagnosis for male and female patients was different ($P < 0.001$, Wilcoxon rank-sum test). The distinct trends in age at diagnosis across genders is presented in **Fig. 2**.

In terms of disease duration for each patient, male patients exhibited slightly longer disease duration on average than female patients ($P = 0.072$; 1,555.2 vs. 1,471.1 days). Furthermore, classification of ICD-10 codes of patients at the index date revealed that most patients received the ICD-10 code M080 at the first diagnosis, referring to JIA of the unspecified type, followed by ICD-10 codes M081 for approximately 8.4% of male patients and M089 for approximately 5.8% of female patients.

Prevalence

The annual prevalence rate per 100,000 individuals of JIA across the overall population and within the four subgroups according to age over a 10-year period (2010–2019) is presented in **Fig. 3A**. The annual prevalence rate in the overall population was 15.9 (range, 14.5–16.8), exhibiting a gradual decrease. Furthermore, a clear trend of the annual prevalence rates increasing with age was observed. Notably, the adolescent subgroup consistently had the highest annual prevalence rate, suggesting a higher incidence of JIA among adolescents. The annual prevalence rate in the male population was 15.4 (range, 13.1–17.0) (**Fig. 3B**); moreover, patterns similar to that in the overall population were evident, with a decreasing

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Table 1. Demographics of the study population (N = 1,728)

Variables	Sex		*P* value
	Male	Female	
Total	934 (54.1)	794 (45.9)	-
Age at diagnosis	10.7 ± 3.8	9.4 ± 4.6	< 0.001
	12.0 (1.0–15.0)	10.0 (0.9–15.0)	
Disease duration	1,555.2 ± 1,012.6	1471.1 ± 1,024.3	0.072
	1,458.0 (0–3,640.0)	1,335.00 (0–3,644.0)	
Diagnosis code (%)			0.289
M08	1 (0.1)	0 (0.0)	
M080	654 (70.0)	631 (79.5)	
M081	78 (8.4)	19 (2.4)	
Systematic			
M082	52 (5.6)	44 (5.5)	
Enthesitis-related arthritis			
M083	13 (1.4)	15 (1.9)	
Oligoarticular JIA			
M084	19 (2.0)	6 (0.8)	
M088	24 (2.6)	13 (1.6)	
M089	55 (5.9)	46 (5.8)	
Combination	38 (4.1)	20 (2.5)	

All values are calculated on the basis of the observation at the index date. Values are presented as number (%), mean ± standard deviation, or median (min–max).
P values from Wilcoxon rank-sum test.
M08 = juvenile arthritis, M080 = juvenile rheumatoid arthritis with or without rheumatoid factor, M081 = juvenile ankylosing spondylitis, M082 = juvenile arthritis with systemic onset, M083 = juvenile polyarthritis (seronegative), M084 = pauciarticular juvenile arthritis, M088 = other juvenile arthritis, M089 = juvenile arthritis = unspecified, JIA = juvenile idiopathic arthritis.

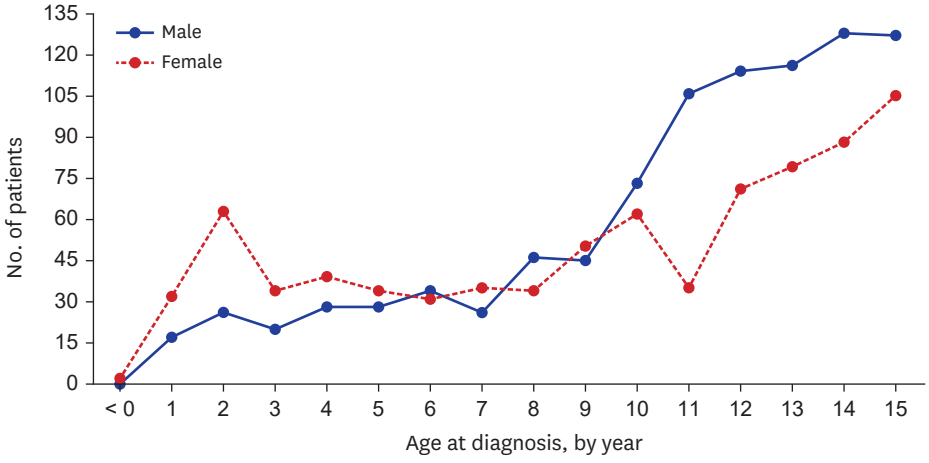

Fig. 2. Number of patients diagnosed at each age by gender.

trend in the annual prevalence rate across all male patients and higher rates in the adolescent subgroup. The female population had an annual prevalence rate of 16.4 (range, 15.9–16.9), which was slightly higher than that of the male population (**Fig. 3C**). Consistent with the rates of the overall and male populations, the annual prevalence rate increased with the age of the female population. However, the female population exhibited more variabilities in the annual prevalence rate across the four age subgroups and did not follow a consistent downward trend. Contrary to the male and overall populations, the annual prevalence rate in the female population had a relatively flat trajectory. A noteworthy observation was the uptick in the annual prevalence rates in the adolescent subgroup between 2014 and 2016 across the overall, male, and female populations, followed by a decline after 2016–2017. The detailed annual prevalence rates are presented in **Supplementary Table 1**.

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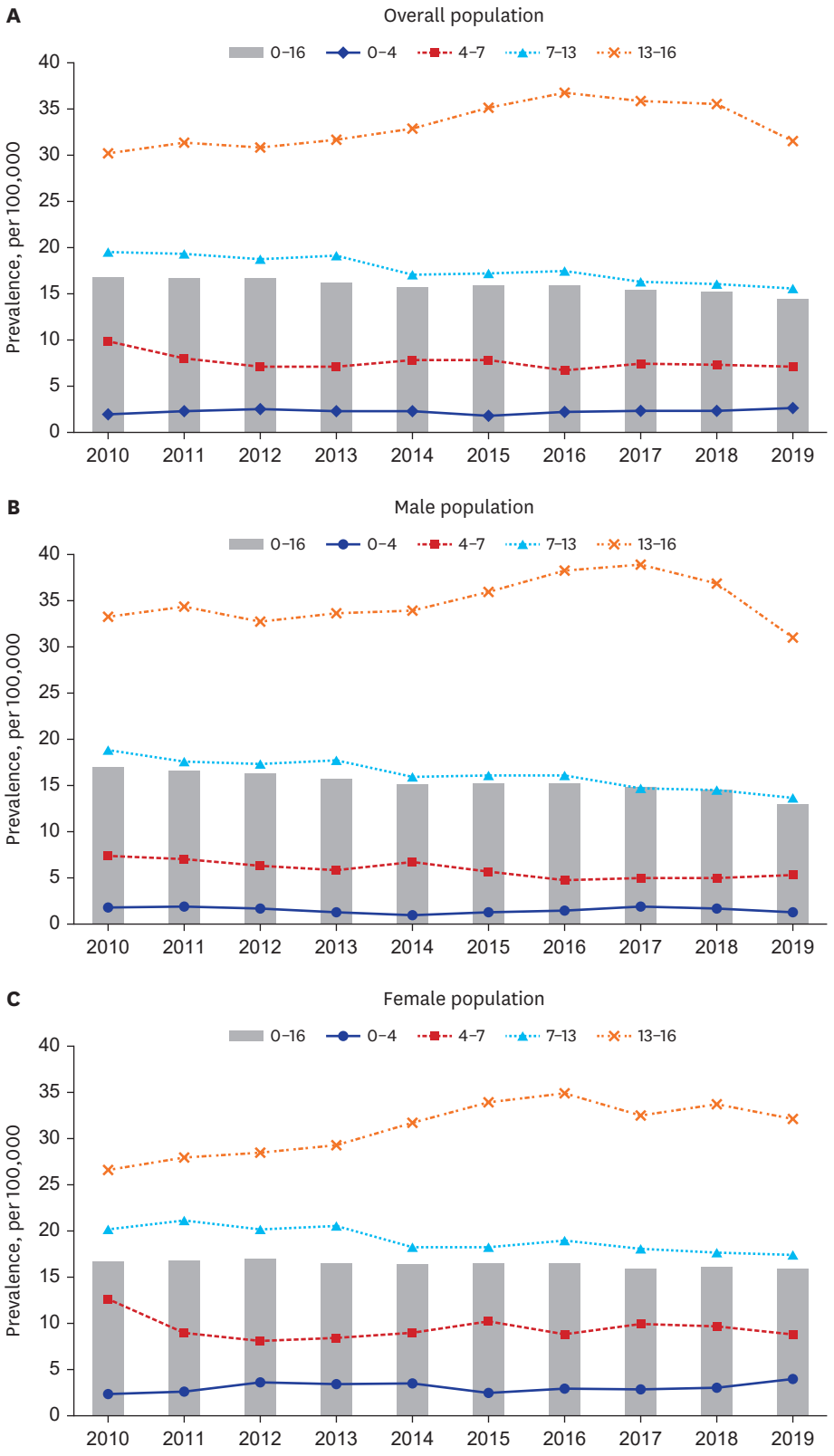

Fig. 3. Annual prevalence rate per 100,000 individuals for each age group. (**A**) Overall, (**B**) male, and (**C**) female populations. Age subgroups: toddler, < 4 years; preschool age, 4–7 years; school age, 7–13 years; adolescent, 13–16 years.

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Incidence

The annual incidence rate of JIA over the study period (2010–2019) is provided in **Fig. 4**. For the overall, male, and female populations, the annual incidence rate of JIA was 2.2 (range, 1.8–2.8), 2.3 (range, 1.7–2.9), and 2.1 (range, 1.8–2.6) per 100,000 individuals, respectively.

Consistent with the annual prevalence rate, the annual incidence rates increased with age across the overall (**Fig. 4A**), male (**Fig. 4B**), and female (**Fig. 4C**) populations. Specifically, the adolescent subgroup consistently exhibited the highest picks, presenting with the highest annual incidence rates across all age subgroups. However, in contrast to the annual prevalence rate, no monotonic trend was noted for the annual incidence rates. The temporal trends of the age subgroups and the overall group were markedly varied. Particularly, the female population exhibited more pronounced fluctuations across the study period with no clear monotonic trend within any single age subgroup. Notably, for the toddler subgroup, the annual incidence rates in the male population were consistently lower than that in the female population for most years. Conversely, for the school age and adolescent subgroups, the female population tended to exhibit lower annual incidence rates than the male population for most years. The detailed annual incidence rates are presented in **Supplementary Table 2**.

DISCUSSION

This study presents pioneering findings on the disease patterns, including the annual prevalence and incidence rate, of patients with JIA through the analysis of population-based large-scale claims data in Korea. The annual prevalence rate was 15.9 (range, 14.5–16.8) per 100,000 individuals and the annual incidence rate was 2.2 (range, 1.8–2.8) per 100,000 individuals. Our values were different from those reported in previous studies. Moreover, the prevalence and incidence rates of JIA were significantly varied in the literature across various regions, ethnicities, and time period. Harrold et al.[21] reported that the age- and gender-standardized prevalence and incidence rates of JIA per 100,000 person-year calculated using the Kaiser Permanente Northern California Autoimmune Disease Registry were 44.7 and 11.9, respectively. Thierry et al.[11] reported that the overall pooled prevalence and incidence rates among Caucasians were 32.6 and 8.3, respectively. Horneff et al.[22] reported much higher values, with overall prevalence and incidence rates of 133.21 and 34.17, respectively, in the WIG2 database and 167.76 and 59.99, respectively, in the InGef database in 2018. Conversely, another study using Taiwan's NHI database reported a much lower prevalence rate of 3.7 per 100,000 individuals, which was significantly lower than our findings and those in Caucasian or German populations.[23] In 1994, the prevalence rate of JIA in Japan was even lower at 0.83 per 100,000 individuals.[24] A study in Taiwan selected its cohort using ICD-9-CM code 714.0 for chronic inflammatory arthritis from 1995 to 1999; however, this represents a limitation as it does not fully align with the more recent JIA-specific ICD-10 codes. Similarly, a Japanese study collected data from a survey conducted for pediatric departments in 1,290 hospitals with over 100 beds from 1984 to 1994. Consequently, both these studies may have underestimated the true incidence of JIA. These variations highlight potential disparities in the prevalence and incidence rates of JIA across countries and emphasize the influence of various factors on these rates, including geographic locations, ethnicities, and additional variables such as comorbid conditions and healthcare access. It is also important to consider that differences in definitions may significantly contribute to variations in reported outcomes.

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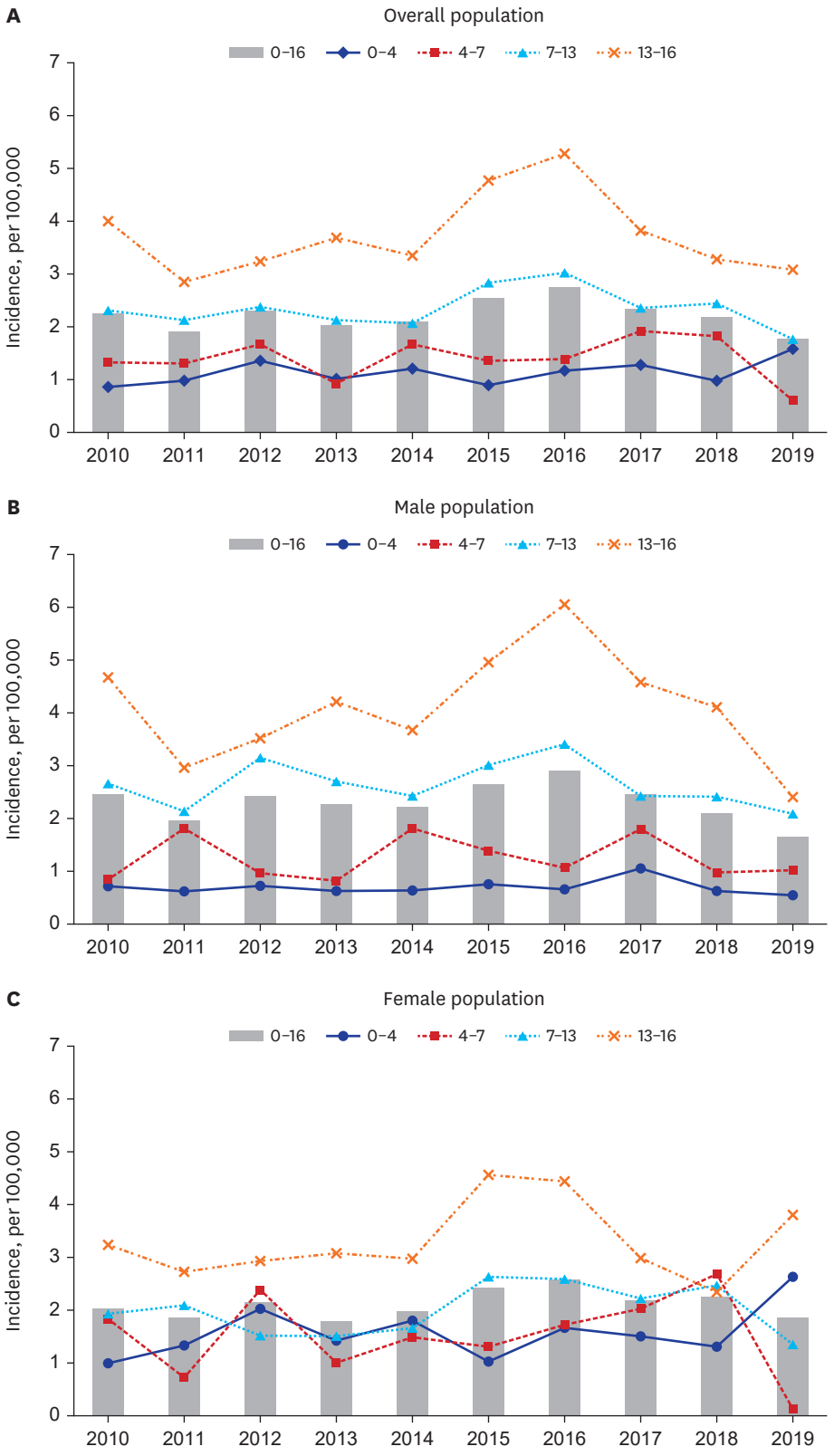

Fig. 4. Annual cumulative incidence per 100,000 individuals for each group. (**A**) Overall, (**B**) male, and (**C**) female populations. Age subgroups: toddler, < 4 years; preschool age, 4–7 years; school age, 7–13 years; adolescent, 13–16 years.

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Our results exhibit slight differences between the male and female populations. The female population exhibited a slightly higher annual prevalence rate (16.4 per 100,000 individuals) across all ages subgroups than the male population (15.4 per 100,000 individuals), whereas the annual incidence rate was similar to that in the male population (2.1 vs. 2.3 per 100,000 individuals, respectively). These findings are contrary to those of several studies reporting that JIA affects females at a much higher rate than males in the western region. Several studies have repeatedly reported gender disparities in terms of prevalence and incidence rates.[11,25-27] Thierry et al.[11] reported substantially different pooled prevalence and incidence rates between genders, with 19.4 and 10.0 for females and 11.0 and 5.7 for males per 100,000 individuals. Similarly, Harrold et al.[21] documented that the prevalence and incidence rates were 61.6 and 16.4 for females, which are much higher than the rates of 28.6 and 7.7 in males per 100,000 individuals. Thomschke et al.[25] reported relatively less gender disparities, with females exhibiting a 1.89-fold higher prevalence rate than males among patients aged < 14 years.

An interesting observation is that although the prevalence and incidence rates for males were predominantly higher in the adolescent subgroup, the younger subgroups (toddler, preschool, and school age subgroups) exhibited higher rates among females. This suggests a gender disparity between the two subpopulations, influencing the observed epidemiological trends. **Fig. 2** elucidates the mechanisms that may contribute to a higher diagnosis rate in males around the age of 10 years. This difference may be due to differences in incidence rates by gender among JIA subtypes. Typically, oligoarticular JIA is more common among females and is most prevalent in early childhood, whereas the enthesitis-related subtype occurs more frequently in males, with peak incidence in adolescence. Although our study could not assess gender-specific incidence rates for each subtype, the observed gender-specific disparities in disease patterns warrant deeper investigation to elucidate the underlying biological, environmental, and potentially latent mechanisms underlying the varying diagnosis rates among subtypes across distinct age groups. Additionally, sociocultural factors may play a role in influencing the diagnosis rates across different age demographics, and these need to be comprehensively examined.[4]

A general trend of increasing annual prevalence rate across all age categories was observed, which is characteristic of chronic conditions that tend to accumulate over time. The adolescent subgroup consistently exhibited the highest annual prevalence rate throughout the study period for the overall and gendered populations. Notably, in 2016, a significant peak in the annual prevalence rate was observed for this age group across the overall, male, and female populations. This finding reveals a potential surge in the annual incidence rates in 2016 for unspecified reasons.

For the overall and male populations, the annual incidence rates tended to increase with age. A consistent finding was that the adolescent subgroup exhibited the highest annual incidence rates for nearly the entire study period. This finding aligns with those of Horneff et al. who reported that patients aged 12–15 years exhibited higher incidence rates than those in the younger age groups (2–5 and 6–11 years) across both databases they analyzed.[22] Similarly, Thomschke et al.[25] reported that the incidence rates among adolescents aged 15–19 years was 1.2-fold higher than that in the group aged 0–14 years. However, an interesting discrepancy in the female population was observed, where the annual incidence rates did not consistently align with age, showing no clear increasing trend. This discrepancy in the trends of prevalence and incidence rates, particularly in the female population, merits further investigation to elucidate the factors underlying these patterns.

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In conclusion, this study conducts a foundational analysis of disease patterns, including annual prevalence and incidence rates, among patients with JIA using population-based claims data in Korea. Our findings not only clarify the current landscape of JIA in Korea but also provide valuable insights into the prevalence and incidence trends across the broader Asian region.

Additionally, this study examines the dynamics of JIA by age and gender, offering insights into disease progression, gender-specific susceptibilities, and the potential impact of public health interventions. These findings highlight the need for research to expand our understanding of the JIA population and guide future healthcare planning and policy initiatives. Addressing current knowledge gaps through further research is essential to optimize healthcare delivery and resource allocation, and develop long-term management strategies for JIA.

Our study had several limitations. First, the use of national claims data presented inherent limitations in terms of comprehensive data analysis. Data were organized according to ICD-10 codes, making it impossible to precisely distinguish subgroups based on the ILAR classification. Consequently, our analysis was restricted to information relevant to billing purposes, introducing potential selection biases because of uninsured clinic visits and susceptibility to coding errors. Additionally, the clinical aspects of disease patterns could not be examined as the national claims data do not include detailed clinical information on patients. Second, discrepancies in the definitions used to characterize the study population across various studies contributed to heterogeneity within our study cohort compared with others. This variability presents statistical challenges and hampers endeavors to standardize outcomes.

As a natural progression of our study, further subgroup analyses for different JIA types and treatment patterns in JIA populations would be valuable. Although this study primarily focuses on disease patterns, we are conducting additional research to examine treatment patterns in depth. We expect this series of studies on JIA populations to provide insights into the distinct characteristics of JIA subtypes and enable the development of tailored therapeutic approaches to ultimately enhance patient outcomes.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Annual prevalence per 100,000 individuals for each subgroup by age group

Supplementary Table 2

Annual cumulative incidence per 100,000 individuals for each age group

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