Burden of alopecia areata in China, 1990–2021: Global Burden of Disease Study 2021

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Abstract

Background: Research has indicated that the disease burden of alopecia areata (AA) in China exceeds the global average. Therefore, accurate and updated epidemiological information is crucial for policymakers. In this study, we aimed to comprehensively assess the disease burden of AA in China.

Methods: The following four key indicators were utilized: the prevalence of cases; disability-adjusted life-years (DALYs); the age-standardized prevalence rate (ASPR); and the age-standardized DALY rate (ASDR) of AA according to the Global Burden of Disease (GBD) study 2021. We analyzed the epidemiological burden of AA in China during 2021, examined changes between 1990 and 2021, and performed a Bayesian age-period-cohort analysis to predict trends over the course of the next decade (2022–2030). Additionally, a Gaussian process regression model was applied to estimate the relationship between the gross domestic product (GDP) and the ASPR and ASDR of AA at the provincial level between 1992 and 2021.

Results: In 2021, the estimated number of patients with AA in China was approximately 3.49 million (95% uncertainty interval [UI], 3.37–3.62 million); of these patients, 1.20 million (95% UI, 1.16–1.25 million) were male and 2.29 million (95% UI, 2.20–2.37 million) were female. This large number of patients with AA resulted in a total of 114,431.25 DALYs (95% UI, 74,780.27–160,318.96 DALYs). Additionally, the ASPR and ASDR were 224.61 per 100,000 population (95% UI, 216.73–232.65 per 100,000 population) and 7.41 per 100,000 population (95% UI, 4.85–10.44 per 100,000 population), respectively; both of these rates were higher than the global averages. The most affected demographic groups were young and female individuals 25–39 years of age. Slight regional disparities were observed, with the northern and central regions of China bearing comparatively higher burdens. Between 1990 and 2021, the health loss and disease burden caused by AA in China remained relatively stable. The ASPR and ASDR of AA increased with the GDP when the annual GDP was less than 2 trillion Chinese yuan; however, a downward trend was observed as the GDP surpassed 2 trillion Chinese yuan. A slight upward trend in the disease burden of AA in China is predicted to occur over the next decade.

Conclusions: AA continues to be a public health concern in China that shows no signs of declining. Targeted efforts for young individuals and females are necessary because they experience a disproportionately high burden of AA. **Keywords:** Alopecia areata; Disability-adjusted life-years; Global burden of disease; Prevalence

Introduction

Alopecia areata (AA) is a chronic and specific autoimmune disease that affects hair follicles and results in non-scarring hair loss.^[1,2] Globally, AA is prevalent among 0.1–0.2% of the population and is associated with a lifetime risk of 1.7–2.1%.^[3,4] The prevalence of AA varies according to ethnicity, sex, and age and the highest estimated prevalence has been observed in Asian countries.^[5] AA is more common among children and young adults: up to 66% of patients with AA are <30 years of age and 20% are >40 years of age.^[6] The association between sex and AA

Access this article online			
Quick Response Code:	Website: www.cmj.org		
	DOI: 10.1097/CM9.000000000003373		

remains unclear; however, women may be more susceptible. $^{[3,7]}$

Although AA is not life-threatening and causes limited physical discomfort, its sudden onset and chronic relapsing course can impair the physical appearance, thus significantly affecting the patient's mental health and quality of life.^[8,9] Patients with AA are also at increased risk for other autoimmune disorders, such as thyroiditis,

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Chinese Medical Journal 2025;138(3)

Received: 03-06-2024; Online: 22-11-2024 Edited by: Lishao Guo

lupus erythematosus, vitiligo, psoriasis, atopy, and cardiovascular and metabolic disorders,^[10,11] which further increase the disease burden of AA. Additionally, AA is associated with a significant incremental economic burden and productivity loss on a personal level as well as a national level.^[12,13]

The Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2019 estimated that nearly 18.4 million individuals worldwide have AA.^[14] The age-standardized disability-adjusted life-years (DALYs) rate for AA in China in 2019 was 7.86 per 100,000 population, which was higher than the global average, resulting in China being ranked 68 out of 204 countries for AA.^[14] Furthermore, a previous study of six provinces in China showed that prevalence rates varied from 0.17% to 0.45% (average, 0.27%).^[15] Because of China's vast territory and rapid social development, detailed research on the current national and provincial epidemiological characteristics and differences is lacking.

Based on the updated GBD 2021 data, this study aimed to assess the epidemiological data regarding AA in China and its provinces between 1990 and 2021, identify populations at high risk for AA, and predict trends of AA over the next decade.

Methods

GBD study overview and data source

This study was based on data extracted from the GBD 2021 study. The GBD aimed to estimate the global health burden and associated risk factors for different diseases. Estimates of the numbers and rates of deaths, incidence, prevalence, years of life lost, and years lived with disability for 371 diseases and injuries between 1990 and 2021 were included in GBD 2021; additionally, all of these data at the global and regional levels across 204 countries and territories were reported according to age and sex. We obtained GBD estimates of the number of cases, DALYs, age-standardized prevalence rates (ASPRs), and age-standardized DALY rates (ASDRs) for AA between 1990 and 2021 at the national and provincial levels in China according to age and sex, to provide a comprehensive assessment of the disease burden of AA in China.

Estimation of the prevalence and DALYs of AA

A description of the estimation methods used for GBD 2021 has been published;^[16] therefore, we briefly described the framework for the overall burden of AA in this work. During the GBD study, AA was included as a cause of skin and subcutaneous conditions and was identified using International Classification of Disease (ICD)-10 codes L63–L63.9 and ICD-9 codes 704.0–704.9. The prevalence of AA was estimated using a Bayesian meta-regression model (DisMod-MR2.1).

Epidemiological data regarding AA were obtained by performing a systematic review of PubMed. The studies provided representative general population data (samples from clinical trials or dermatology clinics were excluded) regarding the AA prevalence and sufficient information (sample size >100) to be input in the Dis-Mod-MR2.1 model to allow a quality assessment. Since the GBD 2010 was performed, the DisMod-MR has been used to evaluate and pool all available data, adjust systematic bias, and produce estimates with uncertainty intervals (UIs) according to world regions. Estimations were conducted at the following five levels: global, super-regional, regional, country, and subnational (where applicable). The minimum global coefficient of variation was set at 0.1 to improve estimations across all regions. Country coefficients were calculated by using both data and prior information available for that location.^[16] In the absence of data, the coefficient of the parent location was chosen to utilize the predictive power of our covariates in data-sparse situations. When modeling estimates for AA, we assumed zero excess mortality and prior remission with a minimum duration of 7 months. The sex covariate was set to zero to adjust for the higher prevalence of female patients compared with the prevalence of male patients; this was attributable to the fact that more female patients sought health consultations for AA.^[16]

The DALY estimates for AA were associated with the severity level (mild AA and severe AA). The disability weights of mild AA were lower than those of severe AA when the DALYs were estimated for AA.

The input data sources and relevant meta-data used to estimate the disease burden of AA can be retrieved from https://ghdx.healthdata.org/gbd-2021 (Institute for Health Metrics and Evaluation data website).

The estimated rates were reported per 100,000 population, and age-standardized rates were calculated using the GBD world population standard. For each estimate, 1000 draws of the posterior distribution were created, and the 95% uncertainty interval (UI) was calculated based on the 0.0025 and 0.0975 quantiles of the draws.

Data analysis

The prevalence, DALYs, and rates of AA were depicted according to province, age, and sex. Age-standardized rates were used to compare the results according to location, sex, and year. Data from 1990 and 2021 were compared to calculate changes in each outcome. Furthermore, we utilized a Gaussian process regression model to estimate the relationship between the gross domestic product (GDP) and the ASPR and ASDR of AA at the provincial level between 1992 and 2021. The data regarding the annual GDP for each province were obtained from the National Bureau of Statistics (https://www.stats.gov. cn/). Finally, we predicted the ASPR and ASDR between 2022 and 2030 by performing a Bayesian age-periodcohort analysis (BAPC). The BAPC model incorporates the age effect, period effect, and cohort effect to allow for simultaneous assessment of the influences of age, period, and birth cohort on the prevalence and DALYs. To smooth the trajectory, we applied second-order random walk priors to the age, period, and cohort effects.^[17] Vague normal priors were assigned to the intercept, and additional

adjustments were added to account for the variability of the data. All data analyses were conducted using R (version 4.0; R Core Team, Auckland, New Zealand).

Results

In 2021, the estimated number of patients with AA was 3.49 million (95% UI, 3.37–3.62 million) in China [Supplementary Table 1, http://links.lww.com/CM9/C212]; of these patients, 1.20 million (1.16–1.25 million) were male and 2.29 million (2.20–2.37 million) were female. This disease resulted in a total of 114,431.25 DALYs (95% UI, 74,780.27–160,318.96 DALYs). The ASPR of AA was 224.61 per 100,000 population (95% UI, 216.73–232.65 per 100,000), which was higher than the global average of 215.01 per 100,000 (208.33–221.75 per 100,000). The ASDR was 7.41 per 100,000 (95% UI, 4.85–10.44 per 100,000), which also exceeded the global average of 7.02 per 100,000 (95% UI, 4.56–9.94 per 100,000).

At the provincial level, we observed large variations in the prevalence and DALYs of AA in 2021 [Supplementary Table 1, http://links.lww.com/CM9/C212]. The three provinces with the largest number of patients with AA were Guangdong, Shandong, and Henan, with 0.32 million (95% UI, 0.31-0.33 million), 0.24 million (95% UI, 0.24-0.25 million), and 0.23 million (95% UI, 0.23-0.24 million) cases, respectively. In contrast, the regions with the lowest number of patients were Macao Special Administrative Region, Xizang, and Qinghai, with 1.86 thousand (1.80-1.93 thousand), 9.09 thousand (95% UI, 8.75–9.44 thousand), and 14.52 thousand (95% UI, 14.01–15.05 thousand) cases, respectively. Guangdong recorded the highest DALYs in 2021, with 10,555.68 DALYs (95% UI, 6940.06–15,113.90 DALYs), which accounted for approximately 9.2% of the national total. This was followed by Shandong, with 8000.44 DALYs (95% UI, 5188.30-11,513.23 DALYs), which represented approximately 7.0% of the total. Macao Special Administrative Region had the fewest DALYs, with 61.11 DALYs (95% UI, 40.32-87.39), which comprised only 0.05% of the total.

The differences in the ASPRs of AA across provincial levels in China were not obvious. Hong Kong Special

Administrative Region reported the highest rate (233.60 per 100,000; 95% UI, 225.10–242.11 per 100,000), whereas Guangdong reported the lowest rate (221.68 per 100,000; 95% UI, 213.91–229.52 per 100,000) [Supplementary Table 1, http://links.lww.com/CM9/C212]. Similarly, there were no significant variations in the ASDRs among the regions. Hong Kong Special Administrative Region had the highest rate (7.70 per 100,000; 95% UI, 4.99–11.01 per 100,000), and Hainan had the lowest rate (7.30 per 100,000) [Supplementary Table 1, http://links.lww.com/CM9/C212].

In 2021, the age-standardized prevalence and DALYs of AA among different age groups and sexes in China displayed distinct patterns. Nationally, the number of AA cases among female patients was notably higher than that among male patients. The ASDR for female patients was 9.93 per 100,000 (95% UI, 6.47-14.02 per 100,000), which was approximately 1.97 times higher than that for male patients (5.05 per 100,000; 95% UI, 3.30-7.11 per 100,000) [Supplementary Table 2, http://links.lww.com/ CM9/C212]. The prevalence and ASPR of AA revealed similar trends between sexes [Figure 1 and Supplementary Table 2, http://links.lww.com/CM9/C212]. Both the prevalence and ASPR of AA displayed a unimodal distribution pattern, with an increase from birth that rapidly increased after age 15 years and peaked for the 30-34 years age group at 0.49 million cases (0.44–0.54 million cases) and a rate of 405.02 per 100,000 (360.49-449.14 per 100,000). Thereafter, these levels decreased with age. The number of cases slightly increased between the ages of 45 years and 54 years, followed by a continuous decrease.

The variations in DALYs and ASDRs across different age groups exhibited a unimodal trend, similar to that of the prevalence data, with the peak occurring in the 30–34 years age group. The peak DALY was 16,344.47 DALYs (95% UI, 10,261.92–23,679.79 DALYs), and the peak ASDR was 13.49 per 100,000 (95% UI, 8.47–19.55 per 100,000) [Figure 1]. Across all age groups, female patients demonstrated a notably higher standardized prevalence and DALY rates than those of male patients. The three greatest disparities in the prevalence and DALYs between sexes were observed in the 30–34 years, 35–39 years, and 45–49 years age groups, whereas the





largest differences in the ASPR and ASDR were observed consistently in the 30–34 years, 35–39 years, and 25–29 years age groups.

Between 1990 and 2021, the crude prevalence rate and DALYs for AA in China exhibited a gradual increase, followed by a decrease [Figure 2 and Supplementary Table 3, http://links.lww.com/CM9/C212]. The peak crude prevalence rate was reached in 2012, at 254.80 per 100,000 (95% UI, 245.99–264.02 per 100,000), and the peak crude DALY rate was reached in 2011, at 8.40 per 100,000 (95% UI, 5.43–11.82 per 100,000). However, the ASPR and ASDR for AA remained stable nationwide over the past three decades. Additionally, the sex ratio of the AA prevalence has not changed significantly, with female patients consistently accounting for the majority of cases.

The results from Gaussian process regression models showed that between 1992 and 2021, the ASPR and ASDR of AA increased with a higher GDP when the annual GDP was less than 2 trillion Chinese yuan; however, the ASPR and ASDR exhibited a downward trend with the increasing GDP when the annual GDP was greater than 2 trillion Chinese yuan [Figure 3].

As previously mentioned, the ASPR of AA in China remained stable between 1990 and 2021 [Table 1]. A slightly increasing trend in the ASPR is predicted, with estimates potentially reaching 228.92 per 100,000 (95%)

UI, 75.34–382.50 per 100,000) by 2030 [Figure 4]. The ASDR of AA has maintained relative stability over the past three decades [Table 1]. Furthermore, this relatively stable trend of the AA rate is predicted to continue, with an estimated rate of 7.47 per 100,000 (95% UI, 2.50–12.45 per 100,000) by 2030 [Figure 4].

Discussion

Using data from the GBD 2021, we found that the national health loss and disease burden caused by AA in China have remained relatively stable over the past 30 years. This stability may be attributed to the increasing total population and aging of the population in China.^[18,19]

Previous studies have reported that genetic and environmental factors can lead to variations in the risk of AA among different ethnic groups.^[20–22] Despite the vast territory of China, there are minor differences in the disease burden between provinces and cities. Previous studies performed in China and a recent survey based on a medical database in Japan both reported a prevalence rate of 0.27% for AA.^[11,15] Overall, the prevalence of AA among Asian populations appears to be similarly high,^[5] suggesting that genetic factors may play a primary role.

Our study also found that the disease burden was higher in the north and central regions of China, potentially because of environmental factors, such as pollution





Figure 3: Trends of the age-standardized prevalence (A) and DALYs (B) of AA in relation to the GDP at the provincial level in China between 1992 and 2021. AA: Alopecia areata; DALYs: Disability-adjusted life-years; GDP: Gross domestic product.

Table 1: Age-standardized prevalence and DALYs and temporal trends of AA in China between 1990 and 2021.				
Items	1990	2021	Percentage change (%)	
Age-standardized prevalence per 100,000 population (95% UI)	224.82 (216.93–232.89)	224.61 (216.73–232.65)	-0.0009 (-0.0015 to -0.0004)	
Age-standardized DALYs per 100,000 population (95% UI)	7.40 (4.84–10.48)	7.41 (4.85–10.44)	0.0015 (-0.0205 to 0.0231)	

AA: Alopecia areata; DALYs: Disability-adjusted life-years; UI: Uncertainty interval.



and climate, as well as the rapid pace of life and mental stress.^[23-25] Conversely, the northwest region experienced a lower disease burden, possibly because of its underdeveloped socioeconomic status, inadequate healthcare system, or other sociocultural factors, which lead to the under-reporting of AA. Enhancing the awareness of AA, integrating traditional medicine practices, improving access to medical services, and providing financial support are essential to addressing these disparities.

Epidemiological studies across multiple countries have found that the impact of sex on AA remains unclear, and most studies have suggested a higher prevalence among female patients.^[26–28] Our findings also indicate that the disease burden of AA is higher for female patients; this trend has persisted across various times, regions, and age groups. Sex differences may be primarily related to the autoimmune nature of AA, which is similar to that of other autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus;^[29,30] therefore, endocrine factors play a significant role in activating the immune system, and genetic factors may vary between sexes.^[31,32] Additionally, the heightened concern regarding physical appearance among female patients and their greater likelihood of seeking medical assistance may further explain these results.^[33]

AA can occur at any age; however, it primarily affects children and young adults.^[19] This study showed that the disease burden is most significant among young adults 25–39 years of age, particularly those 30–34 years of age. This finding is consistent with global research that has suggested that AA imposes a heavy burden on young populations. Social pressures, professional challenges, and lifestyle factors specific to this age group may contribute to this trend. Therefore, focusing on the disease burden among young individuals, especially female individuals, is crucial to mitigating the impact of AA in China.

Our study revealed that the disease burden of AA increased with economic development in regions with an annual GDP less than 2 trillion Chinese yuan. This could be attributable to improved healthcare access and health awareness as the GDP increased in regions that are less developed. However, in regions where the annual GDP exceeded 2 trillion Chinese yuan, the ASPR and ASDR showed a downward trend, suggesting that further economic development as well as improvements in public health measures and health education and increased medical resources may help reduce the disease burden of AA.

Preventive strategies for AA should focus on modifying environmental or behavioral factors, because persistent changes in these factors can alter genetic susceptibility to autoimmune diseases.^[31] Oxidative stress has been preliminarily investigated as a factor associated with the pathogenesis of AA, and exposure to pathogens, such as severe acute respiratory syndrome coronavirus 2 and hepatitis B virus, can also increase the risk of AA.^[21,34,35] Furthermore, lifestyle factors, including smoking, sleep disorders, overweight, and obesity, are strongly associated with the occurrence of AA. Studies have shown that nutritional and caloric excess can overstimulate T lymphocytes, thus leading to the loss of immune privilege.^[36–38] By avoiding or mitigating these risk factors, the burden of AA can be reduced to some extent.

The understanding of the immunomechanisms of AA has deepened, and the clinical application of small-molecule drugs, such as Janus kinase inhibitors, has greatly boosted confidence in the efficacy of AA treatment.^[39,40] Therefore, it is possible to reduce the number of AA cases and improve the epidemiological landscape of AA in the future; however, further research is required.

The limitations of this study include the inherent constraints of the GBD data, for which the accuracy of the estimates was influenced by the quality and availability of primary data. Because hospital and claims data were not included, the true prevalence may have been underestimated. Additionally, this study did not stratify patients by the severity of hair loss, which could have affected the disease burden assessment. Furthermore, the measured disease burden did not account for other potential effects associated with AA (e.g., quality of life, psychological status, and economic effects). The burden of AA should be comprehensively considered by combining the results of this study with other perspectives. Finally, because of limitations during data collection for GBD 2021, this study could not reflect changes in disease burden after the application of Janus kinase inhibitors for AA treatment.

In conclusion, over the past 30 years, the overall burden of AA in China has been stable, with slight growth anticipated during the next decade. These findings suggest that more attention should be focused on young and female individuals. Public health strategies should aim to enhance the diagnostic accuracy and treatment efficacy associated with AA, improve medical insurance coverage, and allocate healthcare funds for AA to gradually reduce its disease burden in China.

Acknowledgments

We appreciate the GBD 2021 collaborators for their work.

Funding

This study was supported by grants from the National Natural Science Foundation of China (Nos. 82073459, 82373504, and 81602939), and by the Capital's Funds for Health Improvement and Research (No. 2020-4-4087).

Conflicts of interest

None.

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How to cite this article: Li XQ, Liu HX, Ren WH, Zhu QJ, Yin P, Wang LJ, Zhang JZ, Qi JL, Zhou C. Burden of alopecia areata in China, 1990–2021: Global Burden of Disease Study 2021. Chin Med J 2025;138:318–324. doi: 10.1097/CM9.00000000003373