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ORIGINAL RESEARCH

Analysis and comparison of the temporal trends of male infertility in China and globally from 1990 to 2021

Si Yan Miao[1,†], Zhi Xin Liu[2,†], Wen Rui Wu[1,†], Long Hua Luo[1,*], Liang Feng[1,*]

[1]Department of Urology, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University, 330006 Nanchang, Jiangxi, China
[2]Jiangxi Medical College, Nanchang University, 330006 Nanchang, Jiangxi, China

***Correspondence**
mlesiyan@email.ncu.edu.cn
(Liang Feng);
ndyfy03660@ncu.edu.cn
(Long Hua Luo)

[†] These authors contributed equally.

Abstract

Background: To analyze and compare the prevalence burden, temporal trends, and predictions of male infertility globally and in China. **Methods**: Data on male infertility in China and globally from 1990 to 2021 were collected, organized, and analyzed using the Global Burden of Disease Study database 2021. The Bayesian Age-Period Cohort model was applied to predict the prevalence burden of male infertility globally and in China over the next 30 years. **Results**: Over the past 30 years, the global prevalence burden of male infertility has shown an upward trend, while in China, it has remained relatively stable. Among the 21 regions analyzed, 12 exhibited an increasing trend, with the fastest growth rate observed in the Andean-Latin American region. Conversely, five regions experienced a decline, most significant decrease occurring in sub-Saharan Africa, Eastern region. Among the 204 countries, 85 showed a decline in male infertility burden, with Malawi experiencing the fastest reduction in burden. In contrast, 67 countries experienced an upward trend, the Philippines showing the fastest increase in burden. The highest number of male infertility cases, both globally and in China, occurred in the 35–39 age group. As the Socio-demographic index improved, the disease burden of male infertility initially increased but then began to decline. Over the next 30 years, the global burden of male infertility is projected to continue rising, while in China, it is anticipated to decrease. **Conclusions**: Overall, the global burden of male infertility is generally increasing, with significant regional variations and age-related differences. In China, the situation has been more stable, and the burden is projected to decline, contrary to the global trends. Potential inaccuracies in the data may affect its applicability. The analysis of provinces, subtypes, and risk factors relies on future updates. There is a need for continued attention to relevant policies.

Keywords

Male infertility; Global burden of disease; Time trend analysis; Prediction

Análisis y comparación de las tendencias temporales de la infertilidad masculina en China y a nivel mundial desde 1990 hasta 2021

Resumen

Antecedentes: Analizar y comparar la carga de prevalencia, las tendencias temporales y las predicciones de la infertilidad masculina a nivel global y en China. **Métodos**: Se recopilaron, organizaron y analizaron datos sobre infertilidad masculina en China y a nivel mundial desde 1990 hasta 2021, utilizando la base de datos del Global Burden of Disease Study de 2021. Se aplicó el modelo Bayesiano de Cohorte Edad-Período para predecir la carga de prevalencia de la infertilidad masculina a nivel global y en China durante los próximos 30 años. **Resultados**: En los últimos 30 años, la carga global de prevalencia de la infertilidad masculina ha mostrado una tendencia al alza, mientras que en China se ha mantenido relativamente estable. De las 21 regiones analizadas, 12 presentaron una tendencia creciente, con la tasa de crecimiento más rápida observada en la región andina de América Latina. Por el contrario, cinco regiones experimentaron una disminución, siendo la más significativa en la región oriental de África subsahariana. Entre los 204 países analizados, 85 mostraron una reducción en la carga de infertilidad masculina, con Malawi experimentando la disminución más rápida. En contraste, 67 países experimentaron una tendencia al alza, destacándose Filipinas con el incremento más acelerado en la carga de infertilidad. A nivel mundial y en China, el mayor número de casos de infertilidad masculina se presentó en el grupo de edad de 35 a 39 años. A medida que el indice Socio-Demográfico mejoró, la carga de la enfermedad de la infertilidad masculina inicialmente aumentó, pero luego comenzó a disminuir. En los próximos 30 años, se proyecta que la carga global de la infertilidad masculina siga aumentando, mientras que en China se anticipa una disminución. **Conclusiones**: En general, la carga global de la infertilidad masculina muestra una tendencia ascendente, con variaciones significativas según la región y diferencias relacionadas con la edad. En China, la situación ha sido más estable y se proyecta una disminución de la carga, en contraste con las tendencias globales. Posibles inexactitudes en los datos pueden afectar su aplicabilidad. El análisis de provincias, subtipos y factores de riesgo depende de futuras actualizaciones. Se requiere una atención continua a las políticas relevantes.

Palabras Clave

Infertilidad masculina; Carga global de la enfermedad; Análisis de tendencia temporal; Predicción

1. Introduction

Male infertility refers to a condition in which a childbearing-age couple, engaging in regular sexual activity without using contraception, experiences the inability of the female partner to conceive naturally due to factors affecting the male partner. As a prevalent reproductive disorder in urology and andrology, male infertility not only affects the quality of life of the individual and their family, but also has broader implications for population growth. According to statistical data from the National Bureau of Statistics of China, the natural population growth rate in China has been on a declining in recent years [1]. As China transitions into an aging society, this downward trend in its population is expected to worsen.

A study conducted in 2020 indicated that 8%–12% of couples of childbearing age are affected by infertility, impacting approximately 190 million people globally [2]. Male and female factors each account for about half of these cases; however, male factors have received less attention [3]. Therefore, sufficient attention should be given to the male factors in infertility treatment. Research has found that the quality of male sperm has been on a declining worldwide over the past decade [4, 5]. This decline is linked to various factors such as genitourinary infections, medications, occupation, congenital genetic factors, unhealthy diet [6] and diseases causing secondary male infertility, such as varicocele [7]. These data indicate that challenges related to male reproductive health are becoming increasingly severe. Previously, Huang B *et al*. [8] conducted a comprehensive analysis of the burden and changing trends of male infertility worldwide based on the Global Burden of Disease 2019 database, providing valuable insights into male reproductive health. However, there are currently no detailed reports on the latest global and Chinese population male infertility burden.

The Global Burden of Disease (GBD) database is a comprehensive health impact database led by the Institute for Health Metrics and Evaluation (IHME) at the university of Washington, covering disease, injuries, and risk factors worldwide. We used the latest GBD 2021 data to analyze and compare the burden of male infertility in the global and Chinese populations. This study employs the most recent statistical data to elucidate the current prevalence burden and changing trends of male infertility in both the worldwide and China. The results may provide a foundation and support for raising awareness of male health, advocating for the diagnosis and treatment of male reproductive health, and encouraging greater investment in resources in future.

2. Material and method

2.1 Database version and definition

The 2021 version of the GBD database (https://ghdx.healthdata.org/gbd-2021) encompasses the severity of diseases, injuries and risk factors across different age, gender, and time dimensions in 204 countries and regions worldwide. Nearly 10,000 researchers from 160 countries contributed to updating this database. By accessing disease data from 1990 to 2021, we focused on the burden of male infertility in China and globally. The GBD 2021 provides infertility data for males aged 15 to 49, with coverage in five-year interval. Globally, GBD 2021 categorizes the 204 countries and regions into five Socio-Demographic Index (SDI) intervals: high SDI, high-middle SDI, middle SDI, low-middle SDI and low SDI.

GBD 2021 defines male infertility as the inability to conceive after 5 years of sexual life without contraceptive measures, attributed specifically to male factors rather than other idiopathic causes. The SDI is a comprehensive indicator reflecting the development level of a country or region, encompassing three dimensions: average years of education, total income level and average life expectancy.

The burden of disease from 1990 to 2021 was assessed using the age-standardized prevalence rate (ASPR), and the trend in burden change over the 30-year period was evaluated by the estimated annual percentage change (EAPC) [9]. If both EAPC and 95% confidence interval (CI) are positive, it indicates an upward trend in change; if both are negative, it indicates a downward trend; otherwise, it suggests relative stability.

2.2 Global and regional burden analysis

To examine the global distribution and regional disparities in the burden of male infertility, we created global maps and conducted comparative analyses. The data were grouped by geographic regions as classified in the GBD study. Maps were generated using R (version 4.3.2) with the ggplot2 and sf packages to visualize the disease burden distribution.

2.3 Bayesian age-period-cohort (BAPC) model for forecasting

To project the future burden of male infertility, we employed a Bayesian Age-Period-Cohort (BAPC) model. By employing the Integrated Nested Laplace Approximations (INLA) and BAPC packages in R, this model allowed us to predict the incidence and prevalence of male infertility through 2050. By accounting for the influences of age, period, and cohort effects, the BAPC model offers a comprehensive framework for anticipating future trends in the disease burden.

The Bayesian Age-Period-Cohort (BAPC) model is a widely used statistical method that helps in understanding how factors such as disease incidence, mortality, and social behavior are influenced by individual age, study period and birth cohort. Initially, we constructed a basic framework through the traditional Age-Period-Cohort (APC) model, defining variables related to age, period, and cohort, as well as their respective effects. Utilizing the Bayesian framework, we incorporated prior information by specifying the prior distribution for each parameter.

The advantage of the BAPC model lies in its ability to effectively address collinearity issues, utilize prior information to enhance the robustness of parameter estimation and provide posterior distributions that reflect parameter uncertainty. Compared to traditional regression models, BAPC model is more flexible and explanatory. Additionally, when compared to modern machine learning models, it performs better in terms of effect interpretation and uncertainty handling.

2.4 Statistical analysis

All statistical analyses and data visualizations were conducted using R (version 4.3.2). Descriptive statistics were calculated for all key variables, with results presented as mean and 95% uncertainty intervals (UIs). Within the GBD framework, these 95% uncertainty intervals are typically computed using the percentile method, where the model generates a large number of parameter estimates from posterior distributions produced by Bayesian models or Monte Carlo simulations In trend analyses, p-values less than 0.05 were considered statistically significant.

3. Results

3.1 Global and regional burdens

We analyzed the age-standardized prevalence rate (ASPR) and development trend of male infertility (**Supplementary Tables 1,2**). The ASPR of global male infertility in 1990 was 1158.86 (95% UI: 696.62–1858.35), increasing to 1354.76 (95% UI: 802.12–2174.77) in 2021 (Fig. 1A) [10]. In China, the ASPR of male infertility in China was 1517.39 (95% UI: 834.93–2599.79) in 2019, rising slightly to 1591.79 (95% UI: 886.51–2708.22) in 2021. Overall, the global trend is upward, while China shows relative stability. The global EAPC was 0.50 (95% CI: 0.36–0.64), while the EAPC in China was 0.01 (95% CI: −0.05 to 0.06). Specifically, the number of male infertility cases increased by approximately 23.51 million globally over the 30-year period (Fig. 1B), with an increase of approximately 1.6 million in China, accounting for about 6.81% of the global total. In terms of the affected population, China's share has decreased by 11.03% over the past 30 years.

Based on the analysis conducted according to the SDI classification (Fig. 2), the highest ASPR for male infertility from 1990 to 2021 has consistently been in the high-middle zone, while the lowest ASPR has been in the high zone since 2010. Apart from the low zone, where the ASPR showed a downward trend before rising again, the other regions exhibited a significant upward trend. The EAPC for male infertility in the low-middle zone was 1.00 (95% CI: 0.59–1.41), indicating the fastest growth, with a 164.99% increase in patient numbers compared to 1990 (95% UI: 139.89%–192.97%).

In terms of the GBD regions (Fig. 3), Eastern Europe has consistently maintained the highest ASPR over the 30 years from 1990 to 2021, with ASPRs of 2048.71 (95% UI: 1134.63–3451.39) and 2058.13 (95% UI: 1120.20–3444.23), respectively. The lowest ASPR values during this period were found in Andes-Latin America (396.61, 95% UI: 290.98–521.42) and Australasia (622.98, 95% UI: 363.35–1142.51), respectively. Among the 21 regions, 12 showed an upward trend, with the fastest growth rate observed in Andes-Latin America, with an EAPC of 2.14 (95% CI: 1.76–2.53). Five regions exhibited a downward trend, with the most significant decline observed in Eastern Sub-Saharan Africa, with an EAPC of −1.19 (95% CI: −1.42 to −0.95). The remaining four regions remained relatively stable, namely the Caribbean, Central Sub-Saharan Africa, Southern Latin America, and East Asia.

Among the 204 countries and regions worldwide (**Supplementary Table 2**), Cameroon had the highest

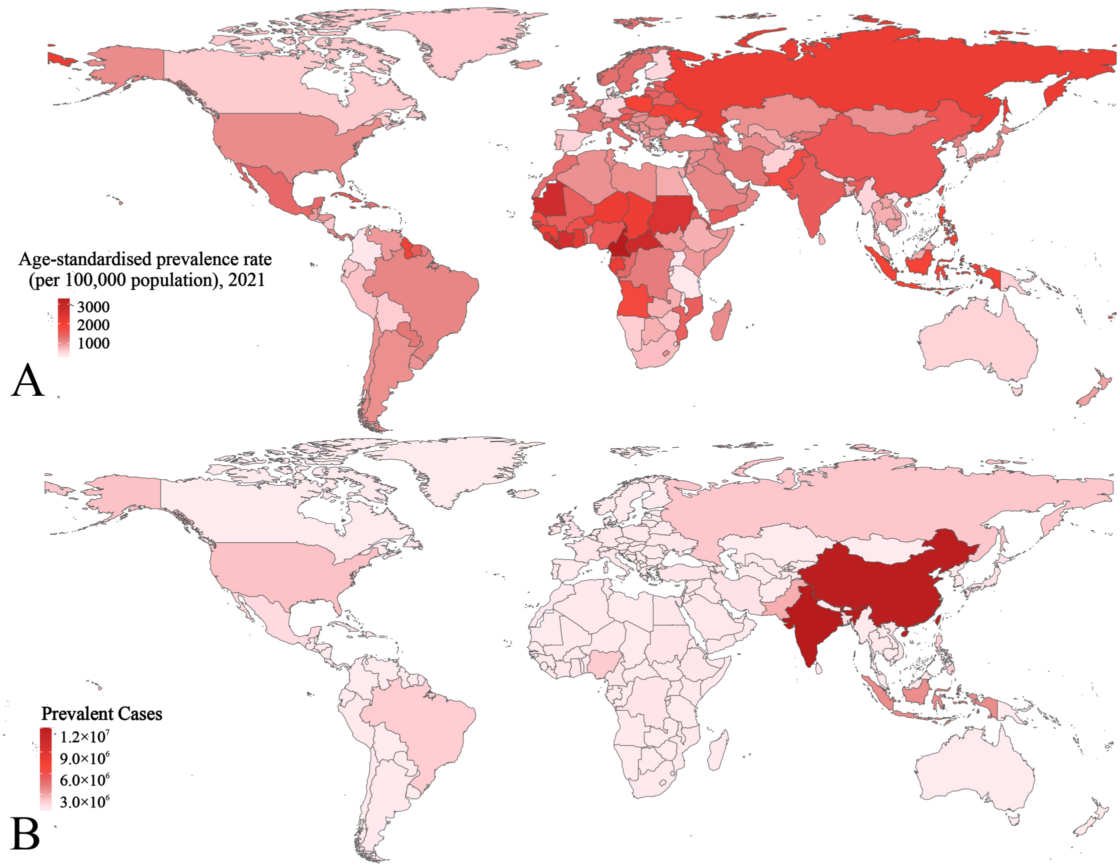

FIGURE 1. Estimated age-standardized prevalence rate and number of patients with male infertility worldwide in 2021. (A) Global distribution map of age-standardized prevalence of male infertility. (B) Global distribution map of male infertility patients.

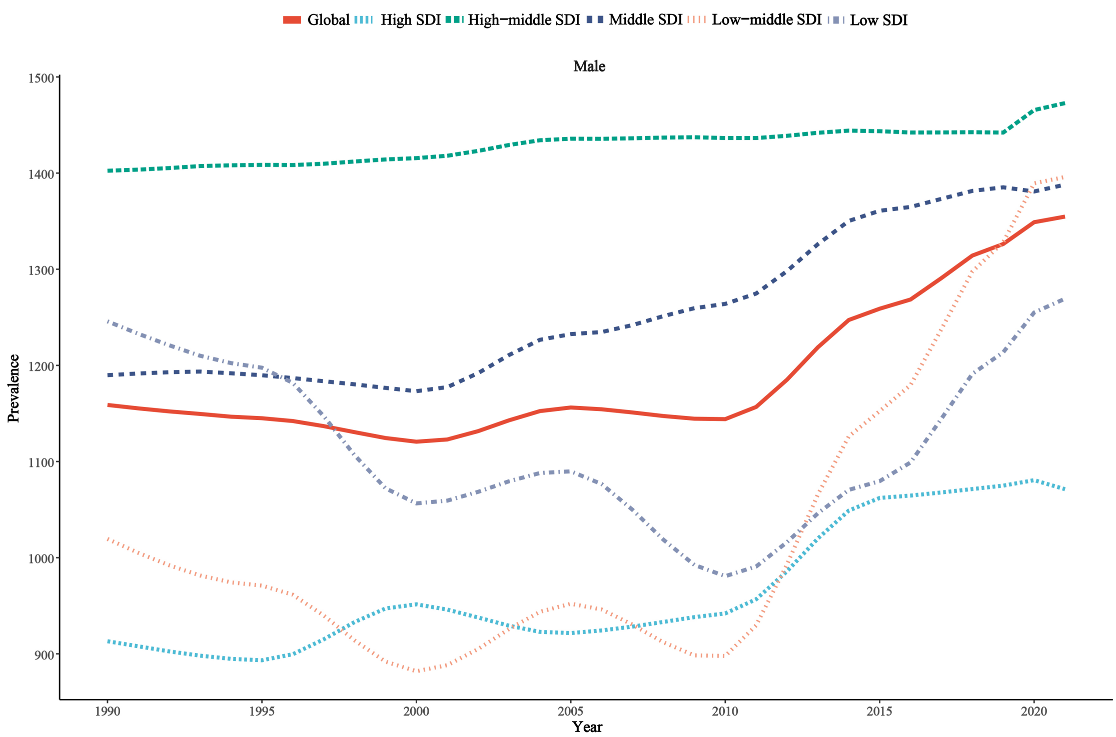

FIGURE 2. Changes in ASPR from 1990 to 2021 across the globe and five SDI regions. SDI: Socio-Demographic Index; ASPR: age-standardized prevalence rate.

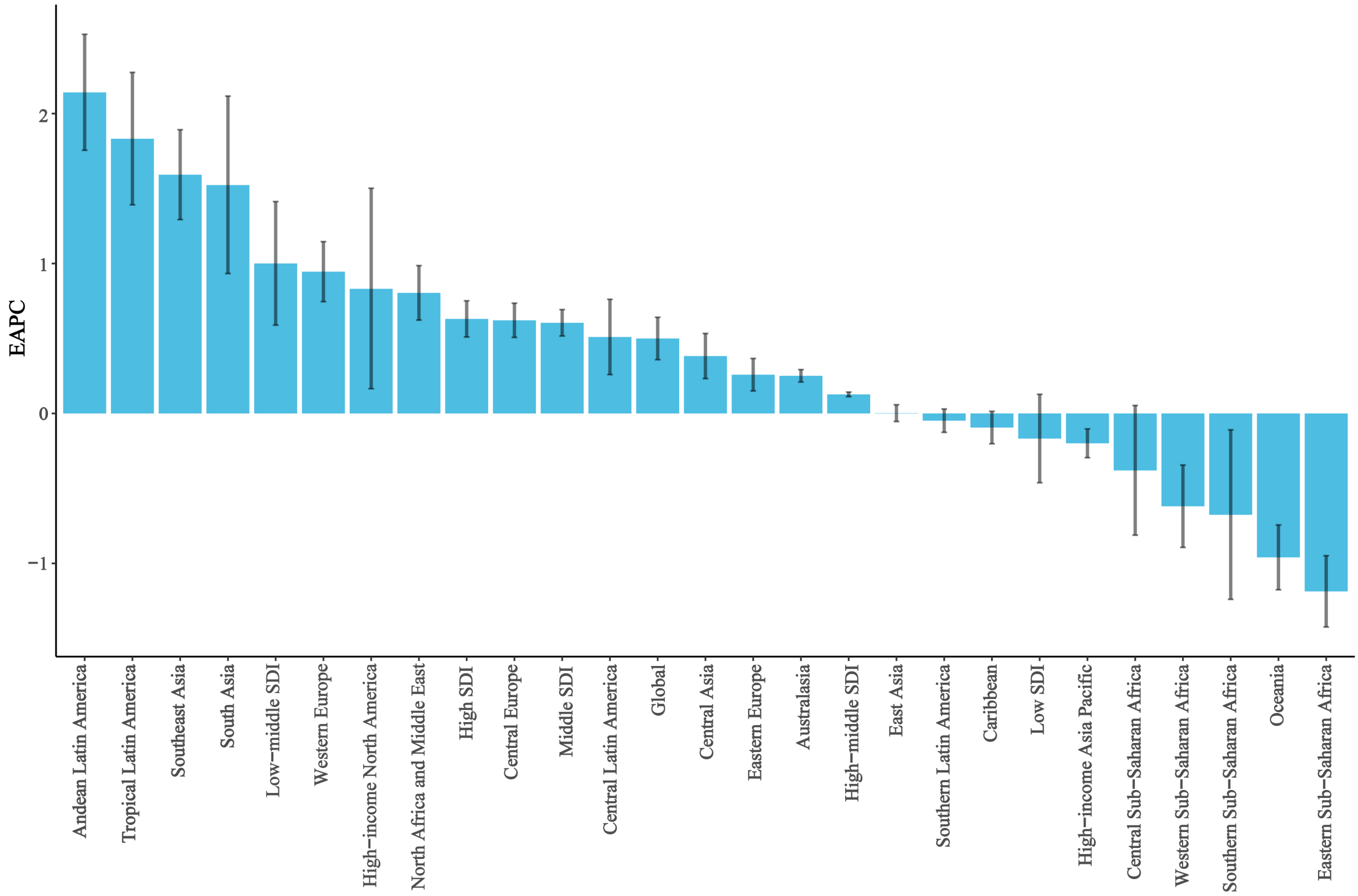

FIGURE 3. EAPC for the global, five SDI regions, and 21 GBD regions. EAPC: Estimated annual percentage change; SDI: Socio-Demographic Index.

ASPR in 1990, while Finland had the lowest. In 2021, Cameroon still had the highest burden, while Burundi had the lowest. Over the past 30 years, 85 countries have shown a downward trend in burden, with Malawi experiencing the fastest decline in burden (EAPC: −4.22, 95% CI: −4.56 to −3.88). In contrast, 67 countries have exhibited an upward trend in burden, with the Philippines experiencing the fastest increase in burden (EAPC: 5.33, 95% CI: 3.18–7.53). The remaining 52 countries have tended to remain relatively stable.

3.2 Age-related analysis

We analyzed the data related to male infertility among individuals aged 19 to 49, as encompassed by the GBD 2021 database. Globally (Fig. 4), the highest number of patients is observed in the 35 to 39 age group, whereas the lowest is found in the 45 to 49 age group. In China (Fig. 5), the highest burden is borne by the 35–39 age group, while the lowest is borne by the 15–19 age group. Regarding the SDI regions (**Supplementary Figs. 1,2,3,4,5**), except for the low-middle region where the 25–29 age group has gradually surpassed the 20–24 age group as the age group with the highest number of patients since 2010. In contrast, the global trend remains consistent across the other regions. The age group with the lowest number of patients in the low-middle region and low region is aligns with the global trend, specifically the 15–19 age group.

3.3 Socio-demographic indicators and male infertility

We also evaluated the correlation between changes in SDI and the prevalence of male infertility (Fig. 6). The analysis revealed that when SDI is below 0.5, the ASPR generally exhibits a downward trend, with the most significant decline observed in Western sub-Saharan Africa. In contrast, when SDI ranges from 0.5 to 0.7, the overall trend shifts upward, particularly in regions such as Western sub-Saharan Africa, the Andean-Latin American region, and Southeast Asia. When the SDI exceeds 0.7, the ASPR generally reflects a downward trend, although some countries, such as high-income North America regions, exhibit a notable pattern of initial decline followed by an increase. Overall, the results suggest that as SDI changes, the disease burden of male infertility patients initially increases and subsequently decreases.

3.4 Burden prediction

From 1990 and 2021, the global prevalence of male infertility has shown an upward trend. In contrast, China experienced an initial increase followed by a decline, resulting in minimal change in the prevalence rate in 2021 compared to 1990. In the estimation for the next 30 years, the global prevalence of male infertility (Fig. 7) is projected to continuous rising, while in China (Fig. 8), a decline is expected to persist.

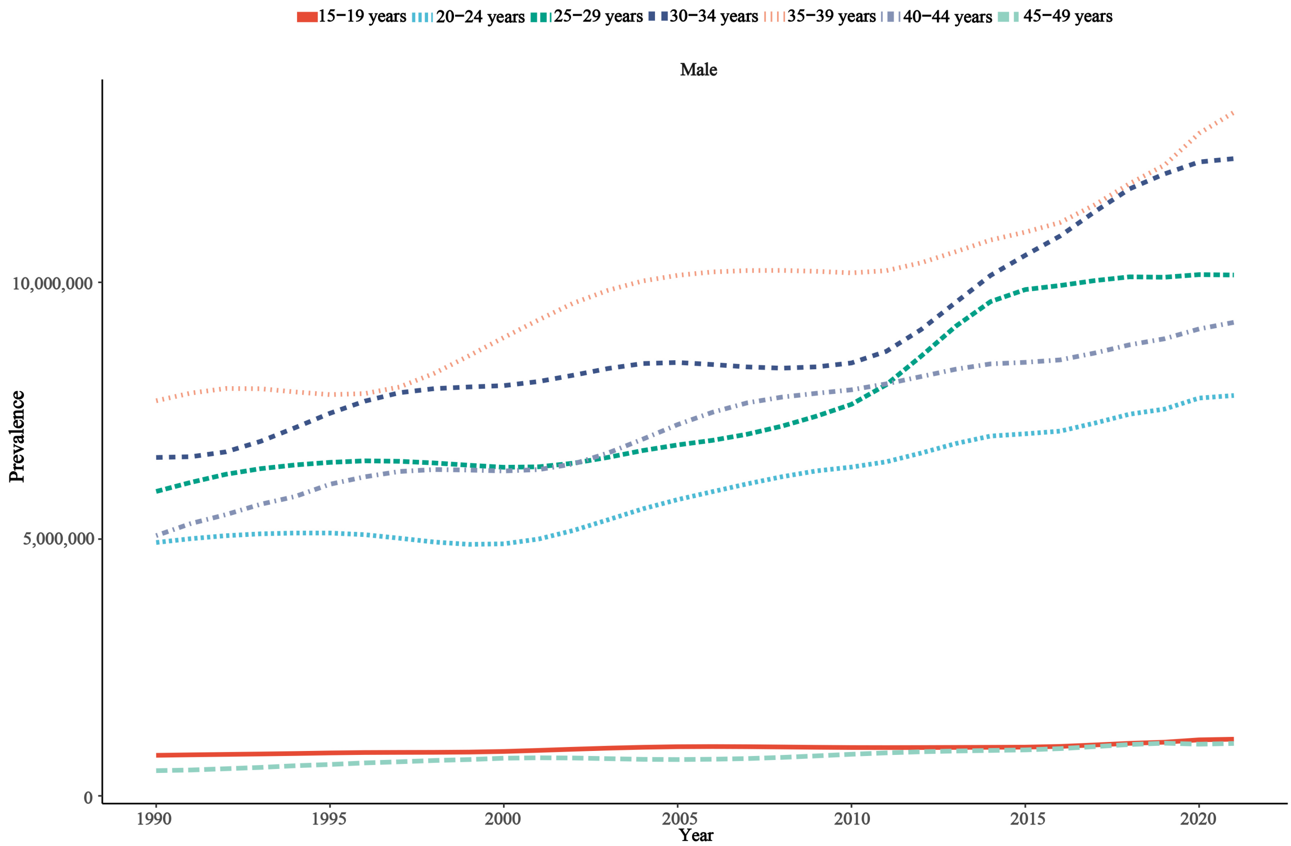

FIGURE 4. Changes in the burden of male infertility among different age groups worldwide from 1990 to 2021.

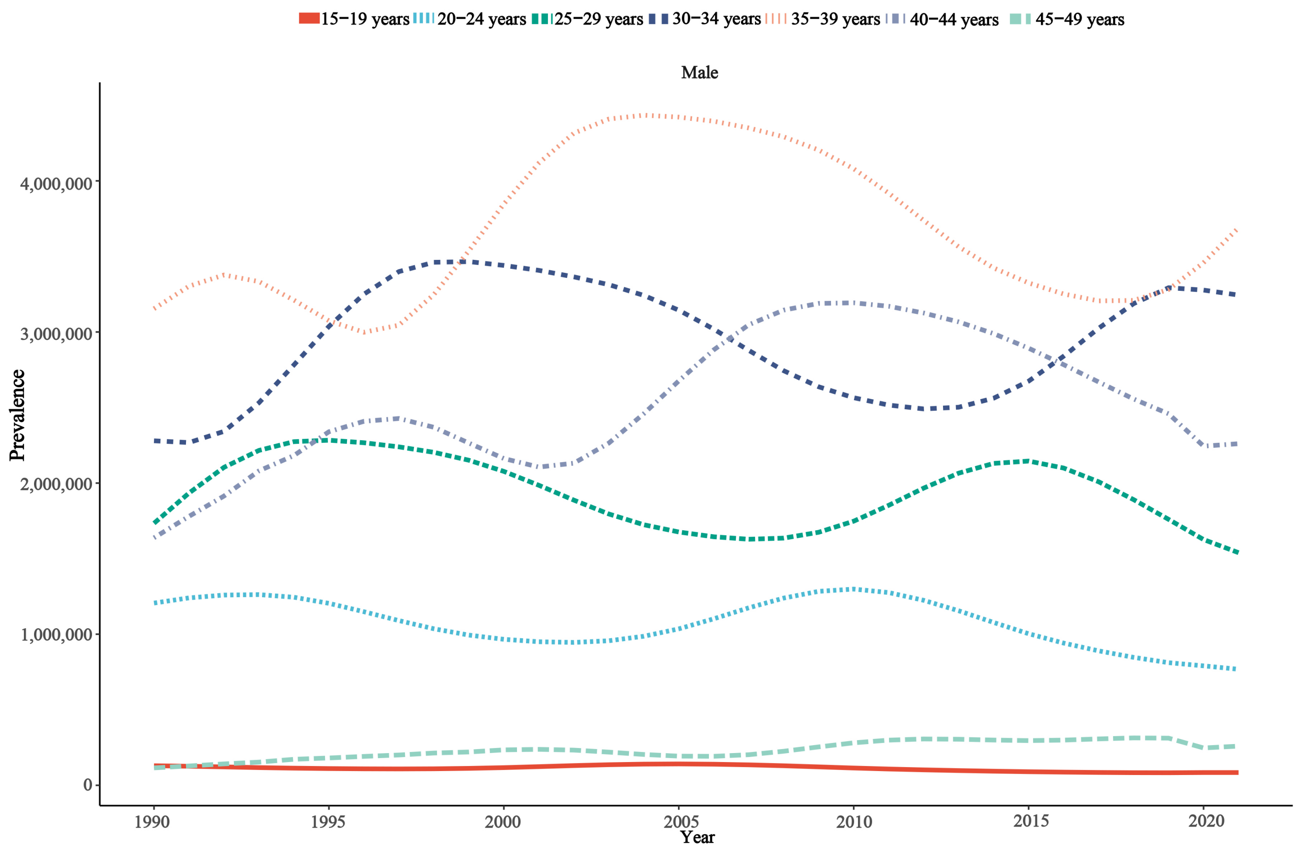

FIGURE 5. Changes in the burden of male infertility in China among different age groups from 1990 to 2021.

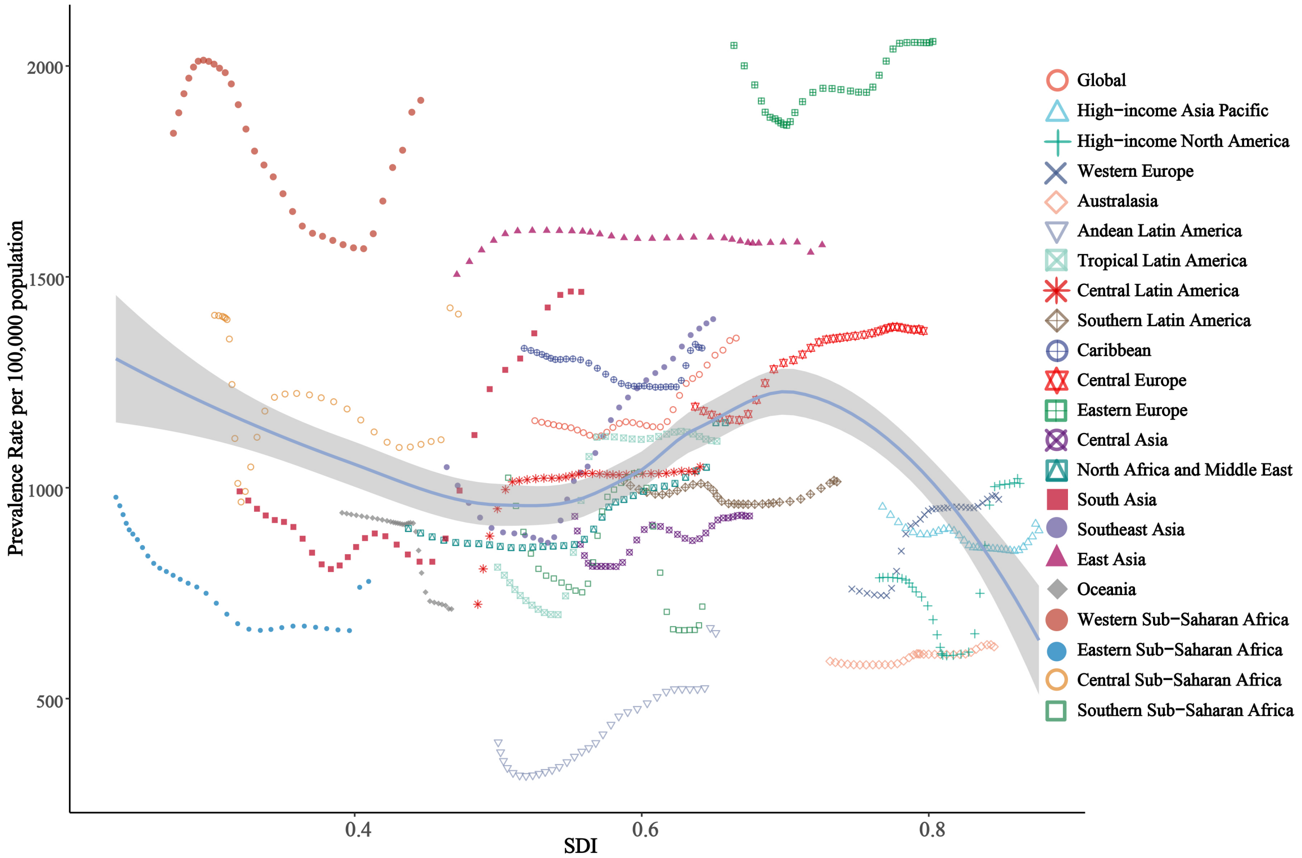

FIGURE 6. Impact of sociodemographic transition on the burden of male infertility. SDI: Socio-Demographic Index.

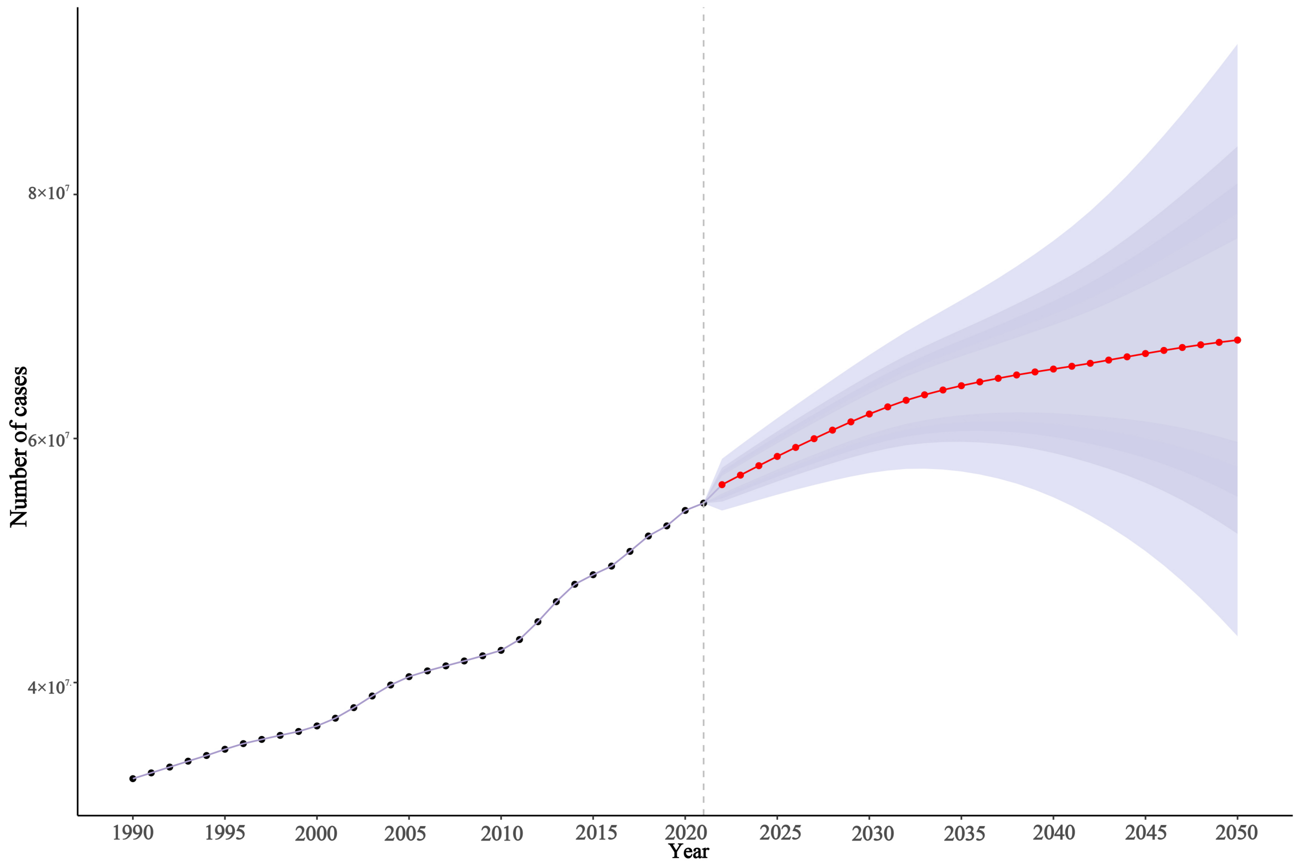

FIGURE 7. Prediction of the global burden of male infertility.

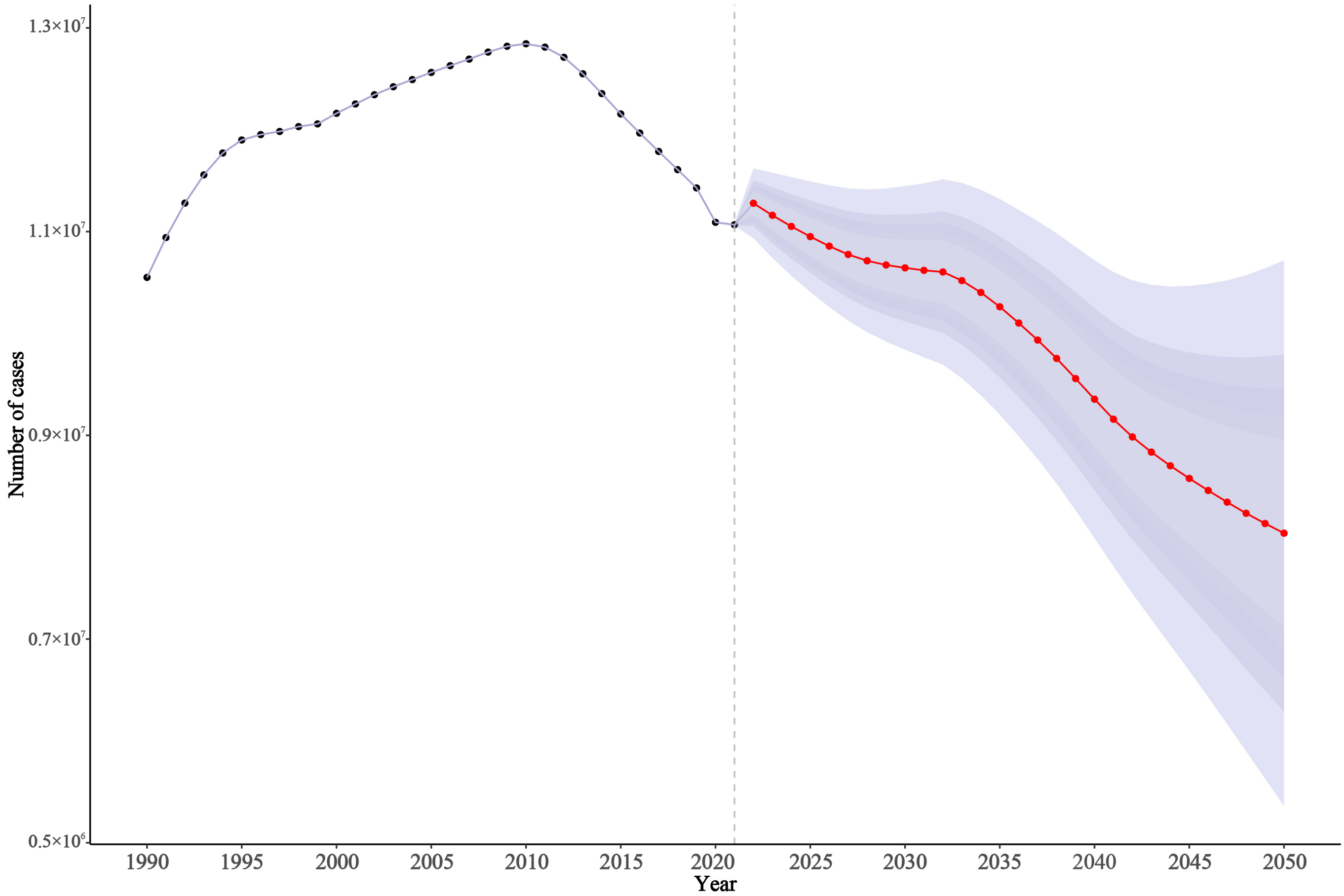

FIGURE 8. Prediction of the burden of male infertility in China.

4. Discussion

Male infertility, defined as female infertility caused by factors related to the male partner, affects the quality of life for countless families worldwide [11]. Approximately two-thirds of male infertility cases can be attributed to identifiable causes, primarily involving pre-testicular, testicular and post-testicular factors. These causes include gonadal dysfunction, congenital genetic and testicular defects, varicocele, ejaculatory system obstruction, and sexual dysfunction [12, 13]. Treatment options for male infertility includes medication, surgery and assisted reproductive technologies, although some empirical treatments and interventions still require validation through randomized controlled trials [14]. Recent basic research has identified potential breakthrough in epigenetics and microbial immunity [15, 16]. However, one-third of male infertility cases remain unexplained making treatment particularly challenging. research suggests that these idiopathic cases may be linked to environment factors, lifestyle and nutrition [17]. Furthermore, the loss and decline in male reproductive capacity is similar to the decline in male sexual function, serving as an indicator of overall male health. Studies have established associations between male infertility and conditions such as testicular cancer and prostate cancer [18, 19], as well as a higher risk of poor overall health and mortality among men [20]. Therefore, comprehending the burden and development trend of male infertility is crucial for emphasizing the importance and urgency of preventing male infertility. Through our collection and analysis of data on male infertility worldwide over the past 30 years, we provide insights into trends and predictions that enhance our understanding of the current burden of male infertility.

Our research results revealed that the prevalence of male infertility is generally been rising globally and across the five SDI regions. Among 204 countries and 21 regions, only 86 countries and 5 regions exhibit a declining trend, underscoring the growing global challenge posed by male infertility. The burden of prevalence varies among different SDI regions. Apart from the high SDI countries, which have consistently maintained a low prevalence, the other four regions exhibit a notable upward trend, with the low-middle SDI region experiencing particularly rapid growth. Previous studies have shown that environmental and dietary factors, such as exposure to microplastics, heavy metals, and adverse effects from industrial food, contribute to a decline in male reproductive capacity [21]. Moreover, rising obesity rates also contribute to a decline in male reproductive capacity [22]. Countries in low SDI regions face significant challenges in environmental governance due to their limited development, while the lower prevalence in high SDI regions can be attributed to more effective environmental management and better disease prevention measures. In China, the EAPC indicates that the ASPR has remained relatively high but stable level over the past 30 years. However, this stability masks an initial increase followed by a decline in the burden of male infertility (Fig. 8). The decreasing trend may be associated with China's increased medical investment and the enhancement of health awareness, leading to a reduced incidence of male infertility caused by diseases such as varicocele. Environmental management and reductions in industrial pollution are also key contributors to this decline. These factors can partially explain the subsequent decline observed in China. Although China's share of global male infertility cases significantly decreased in 2021 compared to 1990, it still accounted for nearly one-fifth of the global total, indicating that male infertility remains a serious concern in the country. According to a statistical report released by the Ministry of Civil Affairs of China, only 7.64 million newlywed couples registered in 2021, with 48.2% of them being over 30 years old. Against this backdrop, reducing the burden of male infertility is particularly important.

We also observed the impact of sociodemographic changes on the male infertility ASPR. Specifically, when the SDI is lower than 0.5, the ASPR tends to decrease. Subsequently, as the SDI increases, the prevalence initially rises and then declines. This finding aligns with previous ASPR analyses conducted across five SDI zones, indicating that the prevalence burden of male infertility is lowest in high SDI regions. Given the diverse cultural, economic, and healthcare conditions across different SDI regions, it is crucial to study and understand these disparities and implement targeted policies to alleviate the burden of male infertility.

Over the past 30 years, more than half of the prevalence burden in 21 GBD regions have experienced an increasing prevalence burden. While the overall increase in the prevalence burden of male infertility in Eastern Europe has not been significant, it has consistently ranked highest, indicating that Eastern Europe still faces significant challenges in the future and needs to increase investment to further reduce the burden. Although Australia had the lowest prevalence burden of male infertility in 2021, it has been on an upward trend over the past 30 years, highlighting the need for vigilance regarding rising prevalence. Compared with other regions, sub-Saharan Africa has been the most successful in combating the prevalence of male infertility. Among 204 countries, 37.84% of developed countries are experiencing an upward trend, 51.35% display downward trend, and 10.81% remain relatively stable. Among developing countries, 31.74% show an upward trend, 39.52% exhibit downward trend, and 28.74% remain stable. The prevalence rate in developed countries has decreased at a higher rate while developing countries have a higher proportion of relatively stable countries. In this context, developing countries hold greater potential in combating male infertility.

We know that female fertility decreases with age, and this change is also observed in males. Studies have found that male sperm quality does not significantly decline until the age of 35 [23]. Castellini C *et al*. [24] identified a significant negative correlation between age and total sperm motility, progressive motility, total progressive motile count (TPMC) and normal sperm morphology. Notably, total sperm motility and progressive motility significantly decreasing in the 40-year-old age group [24]. The older the age, the thicker the basement membrane of the seminiferous tubules [25], the decrease in Leydig cells [26], and testosterone [27]. Our findings revealed that the largest number of male infertility cases worldwide, and in China, occur in men aged 35 to 39. This can be attributed to factors like later marriage [28] and the decline in male fertility with age. In low- and middle-income regions, the age range for male infertility is also increasing. Our research highlights the age-related differences in male infertility burden, which show a trend of increasing age among male infertility patients. Targeted research and investigation into this phenomenon can help develop intervention measures to alleviate male infertility.

We found that there are significant differences in the prevalence burden prediction of male infertility between China and the global trend. Globally, the prevalence burden of male infertility is projected to reach high by 2050, whereas in China, the prevalence is expected to decrease between 2021 and 2050. According to the latest population data from the National Bureau of Statistics of China, the natural population growth rate in China at the end of 2023 was −1.48‰. This negative growth rate could potentially indicate good news for China in terms of addressing its declining population. The predictive accuracy of the BAPC model heavily relies on the quality of historical data. The GBD database has undergone years of updates and improvements, and we have confidence in its data quality as well as in the future predictive outcomes. However, it is important to note that our predictions may still be influenced by uncontrollable factors. Our predictive results still require subsequent verification, and similarly, they necessitate further analysis of the GBD database.

This study explored the distribution and changes in the burden of male infertility, analyzed the specific burden across different regions, countries, and ages, revealed its scale and distribution, and also analyzed global trends from various perspectives. However, this study still has many limitations: the accuracy of data from certain countries or regions may vary, which can impact the estimates of disease burden. Data from China does not include provinces, making comparative analysis relatively simple; diagnostic criteria for male infertility may vary across different countries, and may even differ from the GBD definition, which may have changed over the past 30 years, leading to overestimation or underestimation of cases. Moreover, this study lacks data on disease influencing factors, such as environmental and dietary factors, and targeted analysis of these data may help alleviate the burden. Due to the lack of data on subtypes of male infertility, a detailed analysis of secondary and primary male infertility cannot be achieved, which depends on future updates of GBD data.

5. Conclusions

This study reveals contrasting trajectories in male infertility burden between global and Chinese populations. Globally, the prevalence burden shows a persistent upward trend, projected to intensify over the next 30 years. Significant regional disparities exist: 12 of 21 GBD regions exhibit increasing burdens, while Eastern Sub-Saharan Africa demonstrates the steepest decline. Age stratification identifies the 35–39 cohort as the highest-risk group worldwide, aligning with demographic aging patterns. China presents a distinct profile: despite maintaining relative stability over the past three decades, our projections indicate a forthcoming decline. This divergence likely stems from China's unique socioeconomic transition and healthcare investments. However, potential inaccuracies in the data may impact its applicability, and a more detailed analysis of provinces, subtypes, and risk factors will depend on future data updates. Attention is still needed in formulating relevant policies to address these issues.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and/or analyzed during the current study are available in the (GBD 2021) repository, (https://ghdx.healthdata.org/gbd-2021).

AUTHOR CONTRIBUTIONS

SYM and ZXL—designed the research study. SYM, ZXL and WRW—performed the research. LHL and LF—provided help and advice on research methods. ZXL—analyzed the data. SYM, ZXL, LHL, LF and WRW—wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://files.intandro.com/files/article/1938980352260227072/attachment/Supplementary%20material.docx.

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