BMC Women's Health

RESEARCH

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Changing trends in the global burden of polycystic ovarian syndrome-related infertility over the past 30 years: retrospective data analysis of the global burden of disease study 2019

Ming Huo[1,2†], Yixiang Wang[1,2†], Xianbin Yuan[3†], Yue Yuan[1,2] and Xuehong Zhang[1,2*]

Abstract

Objectives Polycystic ovary syndrome (PCOS) represents a significant and persistent metabolic disorder, emerging as a leading factor contributing to infertility. Despite its profound impact, there remains an inadequate understanding of the global burden of PCOS-related infertility across diverse regions and countries. The aim of this study was to evaluate the global, regional, and national burden of PCOS-related infertility from 1990 to 2019.

Methods The data utilized in this study were derived from the Global Burden of Disease Study 2019. The global burden of PCOS-related infertility was collected and subsequently categorized based on age and sociodemographic index (SDI) spanning the period from 1990 to 2019. Temporal trends in PCOS-related infertility over the past three decades were scrutinized employing joinpoint regression analysis, enabling the determination of annual percentage change (APC) and average annual percentage changes (AAPCs). The association between the age-standardized prevalence rate (ASPR), age-standardized YLD rate (ASYR), and the AAPCs in ASPR and ASYR and the SDI was performed using linear regression analysis. Additionally, the Slope Index of Inequality (SII) and the Relative Concentration Index were employed to assess the inequalities in the distribution of infertility burdens related to PCOS.

Results Globally, the number of prevalent cases and YLDs due to PCOS-related infertility increased from 5,997,589 (95% UI: 3,772,636-8,764,813), and 35,201 (95% UI: 13,282 – 80,010) in 1990 to 12,131,849 (95% UI: 7,625,027 – 17,945,905), and 69,694 (95% UI: 26,756 – 160,420) in 2019, respectively. The age-standardized rates of prevalence and YLDs consistently increased over the same period, with respective AAPCs of 2.45 (95% CI: 2.4–2.5) and 2.37 (95% CI: 2.32–2.43), respectively. The number of prevalent cases and rate of PCOS peaked in the 25–29 years. Populations with high SDI had the highest ASPRs and ASYRs of PCOS-related infertility, while populations with low

†Ming Huo, Yixiang Wang and Xianbin Yuan contributed equally to this work.

*Correspondence:
Xuehong Zhang
zhangxueh@lzu.edu.cn

Full list of author information is available at the end of the article

SDI exhibited more pronounced upward trends. Additionally, linear regression analysis revealed that ASPRs and ASYRs were positively correlated with SDI ($R = 0.419$ and 0.433, respectively, all $P < 0.0001$), and the AAPCs in ASPRs and ASYRs were negatively correlated with SDI ($R = -0.570$ and -0.571, respectively, all $P < 0.0001$). The SII for prevalent cases and YLDs were 121.94 (95% CI: 94.66–149.23) and 0.75 (95% CI: 0.55–0.85) to 146.56 (95% CI: 110.27–182.86) and 0.91 (95% CI: 0.71–1.03), respectively.

Conclusion The prevalent cases and YLDs, along with the ASPRs and ASYRs attributable to PCOS-related infertility, exhibited a consistent upward trajectory over the past 30 years. This escalation was closely associated with factors such as age, socioeconomic status, and geographic location. It is crucial to bolster healthcare management, devise timely and efficacious prevention and control strategies, and provide epidemiological theoretical evidence to alleviate the burden of PCOS-related infertility.

Keywords Infertility, Polycystic ovary syndrome, Global burden of Disease Study 2019, Prevalence, Years lived with disability, Health inequality

Introduction

Infertility not only has a negative influence on an individual's physical and mental well-being but also extends to global public health and socioeconomic development [1]. Infertility is acknowledged as a substantial public health concern by the World Health Organization, with an estimated global prevalence of 186 million couples [2]. According to a 2019 report, the age-standardized prevalence rates (ASPRs) of infertility showed a significant rise of 14.96% from 1366.85 per 100,000 in 1990 to 1571.35 per 100,000 in 2017 [3]. The decrease in fertility rates engenders social challenges, most notably the phenomenon of demographic shift. It is anticipated that by the year 2100, 183 countries will have fertility rates that fall below replacement levels [4]. According to the global projection for 2100, the ratio of individuals aged 65 and above to those under the age of 20 will increase by 1.3 times [4]. The aging of the population will have critical negative repercussions for international development. As a result, initiatives addressing infertility and reproductive health concerns and promoting fertility must be given top priority.

Polycystic ovary syndrome (PCOS), which affects 5–10% of women globally, is one of the most prevalent endocrine disorders among women of reproductive age [5]. 80% of anovulatory infertility can be attributed to PCOS, making it the most prevalent etiology [6, 7]. Besides affecting ovulation, PCOS also can alter primary and secondary oocyte and embryo quality [8], and endometrial competence [9], which increases difficulty in conceiving. Additionally, several research indicates that PCOS and its correlated symptoms may exert an adverse impact on mental health, manifesting as an elevated prevalence of anxiety and depression [5, 10–12], while infertility exacerbates this situation. PCOS-related infertility not only imposes significant psychological stress on individuals but can also have far-reaching impacts on marital relationships, societal roles, and overall well-being. Although PCOS-related infertility is a global problem affecting people around the world, few studies have investigated the topic. A large community-based cohort study showed that infertility affected 47.17% of women with PCOS and 16.42% of women without PCOS [13]. Consistently, PCOS was associated with a 15-fold increased risk of infertility, according to another large community-based cohort study which found that PCOS constituted a substantial proportion (40%) of all women who underwent infertility treatment [14]. These findings suggest that PCOS-related infertility bears a substantial treatment burden in infertility. However, accurate information regarding the burden of PCOS-related infertility is sorely lacking.

To fill these gaps, we conducted an analysis of the burden of PCOS-related fertility in the current study utilizing the most recent data from the Global Burden of Disease Study 2019 (GBD 2019). In this study, we investigated the changes in the global prevalence and years lived with disability (YLDs) of PCOS-related fertility from 1990 to 2019 and assessed the global burden of PCOS-related fertility by age, region, nation, and socio-demographic index (SDI). Our research attempts to afford a greater understanding of the current burden of PCOS-related infertility, providing healthcare professionals, policymakers, and society as a whole with insightful information that promotes the health and well-being of affected women.

Materials and methods

Data sources

The GBD 2019 offers comprehensive insights into the incidence, prevalence, mortality, years of life lost (YLLs), YLDs, and disability-adjusted life-years (DALYs) associated with 369 diseases and injuries across 204 countries and territories from 1990 to 2019. Our data collection focused on extracting prevalence and YLD-related information pertaining to PCOS-related infertility, as well as SDI, directly from the GBD study database accessible at http://ghdx.healthdata.org/gbd-results-tool. Given the

Table 1 Prevalence and years lived with disability of infertility due to polycystic ovarian syndrome and their average annual percentage changes from 1990 to 2019 at the Global and Regional levels

	Prevalence						YLDs					
	Number, 1990	ASPR (per 100 000 Population), 1990	Number, 2019	ASPR (per 100 000 Population), 2019	AAPC, 1990–2019	*P* Value	Number, 1990	ASYR (per 100 000 Population), 1990	Number, 2019	ASYR (per 100 000 Population), 2019	AAPC, 1990–2019	*P* Value
Worldwide	5,997,589 (3772636–8764813)	110.26 (69.64-162.38)	12,131,849 (7625027–17945905)	152.61 (95.88-225.76)	2.45 (2.4–2.5)	< 0.001	35,201 (13282–80010)	0.64 (0.24–1.46)	69,694 (26756–160420)	0.88 (0.34–2.02)	2.37 (2.32–2.43)	< 0.001
SDI Region												
High SDI	2,076,757 (1335904–3010268)	233.39 (149.7-339.85)	2,555,797 (1715986–3632423)	265.4 (177.29-377.18)	0.7 (0.62–0.79)	< 0.001	12,394 (4721–27528)	1.4 (0.53–3.08)	15,135 (5848–33440)	1.58 (0.61–3.45)	0.68 (0.63–0.72)	< 0.001
High-middle SDI	1,212,546 (774018–1782723)	98.36 (62.76-144.08)	2,291,446 (1430364–3424521)	152.8 (95.52-227.94)	2.22 (2.15–2.29)	< 0.001	6998 (2629–15858)	0.57 (0.21–1.28)	12,951 (4907–29988)	0.87 (0.33-2)	2.14 (2.07–2.22)	< 0.001
Middle SDI	1,876,268 (1158361–2848056)	103.03 (63.66-154.72)	4,660,958 (2892764–6937632)	182.85 (113.63-273.14)	3.18 (3.09–3.27)	< 0.001	10,934 (4096–25237)	0.6 (0.22–1.39)	26,627 (10037–62079)	1.05 (0.4–2.43)	3.11 (3.03–3.19)	< 0.001
Low-middle SDI	622,795 (364066–946036)	57.06 (33.56–86.86)	1,916,390 (1153550–2904384)	101.82 (61.38-153.72)	3.94 (3.88–4)	< 0.001	3647 (1362–8470)	0.33 (0.12–0.78)	10,900 (4056–25656)	0.58 (0.22–1.37)	3.84 (3.79–3.89)	< 0.001
Low SDI	205,420 (115948–318552)	43.75 (24.88–67.1)	698,990 (404982–1092276)	64.02 (37.29–99.75)	4.31 (4.26–4.36)	< 0.001	1206 (441–2847)	0.25 (0.09–0.6)	4032 (1508–9553)	0.37 (0.14–0.87)	4.24 (4.18–4.3)	< 0.001
South–East Asia, East Asia, and Oceania												
East Asia	1,051,600 (610398–1623625)	75.65 (44.27-116.92)	2,213,790 (1327469–3358608)	144.58 (87.76-220.38)	2.6 (2.48–2.71)	< 0.001	5675 (2051–13845)	0.41 (0.15–0.99)	11,925 (4359–29486)	0.78 (0.29–1.89)	2.59 (2.47–2.71)	< 0.001
Southeast Asia	643,980 (387320–971635)	135.82 (80.96-204.54)	1,845,023 (1135116–2743963)	251.58 (155.25-375.71)	3.7 (3.62–3.79)	< 0.001	3801 (1416–8957)	0.8 (0.29–1.89)	10,590 (3981–24948)	1.45 (0.54–3.39)	3.6 (3.52–3.68)	< 0.001
Oceania	7225 (4350–10872)	112.4 (67.45-168.41)	22,141 (13340–33502)	161.07 (96.72-244.27)	3.94 (3.87–4.01)	< 0.001	43 (16–99)	0.66 (0.24–1.52)	131 (48–303)	0.95 (0.35–2.22)	3.9 (3.82–3.98)	< 0.001
Sub-Saharan Africa												
Eastern Sub-Saharan Africa	75,173 (42107–115915)	45.19 (25.46–68.93)	242,653 (138860–379077)	60.78 (34.84–94.04)	4.12 (4.09–4.15)	< 0.001	436 (156–1048)	0.26 (0.09–0.63)	1383 (500–3315)	0.34 (0.12–0.81)	4.07 (4.03–4.11)	< 0.001
Central Sub-Saharan Africa	18,808 (10508–29534)	38.56 (21.63–60.75)	74,167 (42477–116253)	59.09 (33.69–92.61)	4.86 (4.83–4.89)	< 0.001	107 (39–255)	0.22 (0.08–0.52)	420 (150–1001)	0.33 (0.12–0.8)	4.81 (4.75–4.87)	< 0.001
Southern Sub-Saharan Africa	42,289 (24246–66611)	79.85 (45.94-124.26)	88,556 (52090–136025)	102.59 (60.3-156.52)	2.58 (2.53–2.64)	< 0.001	248 (91–592)	0.46 (0.17–1.1)	514 (189–1225)	0.59 (0.22–1.41)	2.56 (2.52–2.6)	< 0.001
Western Sub-Saharan Africa	71,770 (39798–112726)	41.06 (22.79–63.87)	292,581 (166409–464477)	67.97 (38.95-107.05)	4.95 (4.91–4.99)	< 0.001	409 (148–980)	0.23 (0.08–0.55)	1651 (594–3965)	0.38 (0.14–0.92)	4.92 (4.87–4.96)	< 0.001
South Asia												
South Asia	571,418 (344248–844600)	53.12 (32.17–78.06)	2,019,708 (1219961–3084013)	102.21 (61.58-156.12)	4.45 (4.4–4.5)	< 0.001	3408 (1274–7827)	0.31 (0.12–0.73)	11,494 (4262–27337)	0.58 (0.22–1.38)	4.26 (4.21–4.31)	< 0.001

Table 1 (continued)

	Prevalence						YLDs					
	Number, 1990	ASPR (per 100 000 Population), 1990	Number, 2019	ASPR (per 100 000 Population), 2019	AAPC, 1990–2019	*P* Value	Number, 1990	ASYR (per 100 000 Population), 1990	Number, 2019	ASYR (per 100 000 Population), 2019	AAPC, 1990–2019	*P* Value
Latin America and Caribbean												
Caribbean	39,416 (23652–59357)	106.5 (63.66–162.1)	65,058 (39081–99974)	135.49 (81.19-208.51)	1.73 (1.67–1.8)	< 0.001	233 (84–539)	0.62 (0.23–1.46)	380 (137–886)	0.79 (0.29–1.84)	1.68 (1.6–1.77)	< 0.001
Central Latin America	344,191 (219004–511862)	214.12 (134.73-321.01)	688,837 (424109–1039581)	259.33 (159.67-391.34)	2.41 (2.36–2.46)	< 0.001	1975 (751–4560)	1.22 (0.47–2.84)	3870 (1454–9289)	1.46 (0.55–3.5)	2.33 (2.27–2.39)	< 0.001
Tropical Latin America	74,697 (43165–113931)	46.83 (27-71.04)	136,173 (80992–209087)	56.04 (33.47–85.7)	2.04 (1.89–2.19)	< 0.001	450 (160–1054)	0.28 (0.1–0.65)	794 (287–1900)	0.33 (0.12–0.78)	1.93 (1.79–2.07)	< 0.001
Andean Latin America	52,468 (36058–73407)	144.28 (98-201.71)	155,263 (103671–221457)	231.33 (154.66-331.22)	3.84 (3.69–4)	< 0.001	296 (115–675)	0.81 (0.32–1.86)	887 (333–1987)	1.32 (0.5–2.95)	3.87 (3.74–4.01)	< 0.001
North Africa and Middle East												
North Africa and Middle East	465,354 (284864–699736)	139.78 (85.23-209.47)	1,286,635 (788268–1931605)	189.29 (115.98-284.74)	3.55 (3.49–3.61)	< 0.001	2965 (1108–6644)	0.88 (0.33-2)	7863 (2959–18073)	1.16 (0.44–2.66)	3.41 (3.32–3.5)	< 0.001
Central Europe, Eastern Europe, and Central Asia												
Central Asia	20,586 (11704–31975)	29.75 (17.1-46.35)	44,054 (26166–69079)	44.14 (26.29–69.55)	2.66 (2.58–2.74)	< 0.001	119 (43–281)	0.17 (0.06–0.4)	252 (90–610)	0.25 (0.09–0.61)	2.63 (2.55–2.71)	< 0.001
Eastern Europe	40,352 (22865–62187)	17.63 (9.9-27.28)	49,089 (27896–74609)	24.5 (13.56–37.54)	0.66 (0.61–0.71)	< 0.001	234 (84–556)	0.1 (0.04–0.24)	284 (100–670)	0.14 (0.05–0.34)	0.64 (0.58–0.7)	< 0.001
Central Europe	20,728 (11458–32642)	16.73 (9.17–26.48)	22,110 (13010–34041)	21.2 (12.42–32.58)	0.22 (0.18–0.26)	< 0.001	117 (42–286)	0.09 (0.03–0.23)	124 (44–298)	0.12 (0.04–0.28)	0.19 (0.15–0.22)	< 0.001
High–income regions												
Southern Latin America	49,953 (29311–77594)	101.26 (59.57-156.76)	114,242 (68753–175200)	165.08 (99.49-251.21)	2.89 (2.85–2.93)	< 0.001	298 (108–723)	0.6 (0.22–1.46)	676 (245–1642)	0.98 (0.35–2.38)	2.85 (2.81–2.9)	< 0.001
Western Europe	1,018,017 (676340–1464423)	254.82 (169.23-366.82)	1,234,639 (783786–1797422)	313.13 (200.8-458.73)	0.65 (0.59–0.72)	< 0.001	6204 (2417–13604)	1.56 (0.61–3.42)	7434 (2852–16726)	1.91 (0.73–4.29)	0.61 (0.53–0.69)	< 0.001
North America	706,094 (433657–1047840)	225.25 (136.98-333.29)	884,375 (591814–1230870)	263.96 (176.84-367.93)	0.76 (0.6–0.93)	< 0.001	4317 (1674–10131)	1.38 (0.53–3.2)	5352 (2125–12388)	1.6 (0.63–3.72)	0.7 (0.62–0.78)	< 0.001

Table 1 (continued)

	Prevalence						YLDs					
	Number, 1990	ASPR (per 100 000 Population), 1990	Number, 2019	ASPR (per 100 000 Population), 2019	AAPC, 1990–2019	*P* Value	Number, 1990	ASYR (per 100 000 Population), 1990	Number, 2019	ASYR (per 100 000 Population), 2019	AAPC, 1990–2019	*P* Value
Australasia	45,403 (25297–72422)	205.63 (114.54-328.31)	67,125 (37863–109797)	243.97 (138.54–399.1)	1.35 (1.24–1.46)	< 0.001	266 (95–645)	1.21 (0.43–2.91)	392 (138–934)	1.43 (0.5–3.42)	1.33 (1.24–1.42)	< 0.001
Asia Pacific	638,066 (387000–953015)	339.37 (208.23-507.54)	585,630 (357270–885306)	350.39 (214.15-528.99)	-0.31 (-0.36 - -0.27)	< 0.001	3598 (1352–8418)	1.92 (0.72–4.46)	3278 (1196–7608)	1.98 (0.73–4.64)	-0.34 (-0.4 - -0.27)	< 0.001

AAPC = average annual percent change; ASPR = Age-standardized prevalence rate; ASYR = Age-standardized YLD rate; YLDs = years lived with disability; SDI = sociodemographic index

publicly available nature of the aforementioned data, obtaining informed consent or seeking ethical approval was deemed unnecessary.

Case definition and study variables

The Disease Modeling-Meta Regression V.2.1 was employed to simulate the epidemiological outcomes associated with PCOS-related infertility. This Bayesian meta-regression framework is extensively utilized in GBD epidemiological modeling [15]. The study outcomes were presented in terms of the number of prevalent cases and YLDs, along with ASPRs and ASYRs attributable to PCOS-related infertility across the years spanning from 1990 to 2019. Additionally, crude prevalence and YLD rates were delineated by age, accompanied by the 95% uncertainty interval (UI). The SDI functions as a comprehensive indicator reflecting a country's economic development status. Computed based on per capita income distribution, average years of education, and fertility rate among women under the age of 25, the SDI ranges from 0 to 1 (low to high), providing a characterization of a country or geographical region's developmental level. The Global Burden of Disease study categorized countries and territories into five SDI levels, namely high, high-middle, middle, low-middle, and low. Infertility is defined as the inability to conceive a child, regardless of the cause, after one year of unprotected sex (without using contraceptives) in couples who want to have a child. This definition encompasses both primary and secondary infertility. PCOS is defined based on NIH criteria, as recommended by the American College of Obstetricians and Gynecologists (ACOG). PCOS is characterized by chronic anovulation (lack of ovulation) and hyperandrogenism (elevated levels of male hormones) in women after excluding secondary causes through hormone measurements or clinical findings. Additionally, inequalities in the distribution of infertility burdens associated with PCOS were measured using the Slope Index of Inequality (SII) and the Relative Concentration Index [16].

Statistical analysis

The analysis of temporal trends in ASPRs and ASYRs related to PCOS-induced infertility was conducted using the Joinpoint regression software, accessible at https://surveillance.cancer.gov/joinpoint/. This model employs segmented regression to capture patterns in the distribution of the disease over time. At each juncture point, the annual percentage change (APC) was computed, accompanied by a 95% confidence interval (CI). Furthermore, the calculation of the average annual percentage change (AAPC), derived from the weighted mean of individual APCs, provided a comprehensive overview of the overall trend during the study period. In summary, a rising rate was observed if both the APC and the lower 95% CI

bound exceeded 0, while a declining rate was indicated if both values fell below 0 [17]. Linear regression analysis was employed to ascertain the relationship between ASPR, ASYR, AAPCs in ASPR and ASYR, and the SDI. The WHO's Health Equity Assessment Toolkit were used to calculate the SII and the relative concentration index. All statistical analyses and data visualization were conducted using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria), Joinpoint Regression Program version 4.9.0.0 (National Cancer Institute, Rockville, MD, USA), and GraphPad Prism 9.0 (GraphPad Software, Inc., La Jolla, CA, USA). A significance level of $\alpha = 0.05$ was used, with $P < 0.05$ considered statistically significant.

Results

Trends of global burden due to polycystic ovarian syndrome-related infertility from 1990 to 2019

Globally, both the number of prevalent cases and YLDs attributed to PCOS-related infertility witnessed a substantial increase from 5,997,589 (95% UI: 3,772,636-8,764,813) and 35,201 (95% UI: 13,282 – 80,010) in 1990 to 12,131,849 (95% UI: 7,625,027 – 17,945,905) and 69,694 (95% UI: 26,756 – 160,420) in 2019, respectively (Table 1). During the period from 1990 to 2019, the number of prevalent cases and YLDs for PCOS-related infertility exhibited a significant increase by 102.28% and 97.99%, respectively. Notably, the age-standardized rates of prevalence and YLDs consistently rose over the same timeframe, demonstrating respective AAPCs of 2.45 (95% CI: 2.4–2.5, $P < 0.001$) and 2.37 (95% CI: 2.32–2.43, $P < 0.001$), respectively (Fig. 1; Table 1).

Age-specific disease burden due to polycystic ovarian syndrome-related infertility

In the GBD 2019, women aged 15 to 49 years with PCOS-related infertility were taken into account. Our analysis examined the age-specific burden, including the number of prevalent cases and YLDs, as well as crude prevalence rates and crude YLD rates of PCOS-related infertility across distinct age groups (Fig. 2). In the year 2019, the count of prevalent cases and crude prevalence rates associated with PCOS-related infertility displayed an increase at 15–19 years of age, reaching a peak at 25–29 years of age. Subsequently, a slight decrease was observed from 35 to 39 years of age, followed by a rapid decline in the 45–49 years age group (Fig. 2). Similarly, the YLD count and crude YLD rates pertaining to PCOS-related infertility exhibited an increase at 15–19 years of age, reaching their peak at 25–29 years of age, and subsequently undergoing a rapid decline in the 45–49 years age group (Fig. 2).

Trends of disease burden due to polycystic ovarian syndrome-related infertility by region and nation

The number of prevalent cases and YLDs, and age-standardized rates of prevalence and YLDs due to PCOS-related infertility in most regions, and countries increased from 1990 to 2019 (Table 1, Table S1). East Asia had the highest number of prevalent cases (2,213,790, 95% UI: 1,327,469-3,358,608) and YLDs (11,925, 95% UI: 4,359 – 29,486) in 2019, followed by South Asia and Southeast Asia. Asia Pacific had the highest age-standardized rates of prevalence (350.39, 95% UI: 214.15-528.99) and YLDs (1.98, 95% UI: 0.73–4.64) in 2019, whereas Central Europe had the lowest age-standardized rates of prevalence (21.2, 95% UI: 12.42–32.58) and YLDs (0.12, 95% UI: 0.04–0.28) (Table 1). Additionally, the ASPRs and ASYRs of PCOS-related infertility showed the maximum increase in Western Sub-Saharan Africa with AAPC of 4.95 (95% CI: 4.91–4.99, $P < 0.001$) and 4.92 (95% CI: 4.87–4.96, $P < 0.001$) between 1990 and 2019, respectively, followed by Central Sub-Saharan Africa and South Asia. In contrast, the largest decline in the ASPRs and ASYRs with AAPC of – 0.31 (95% CI: – 0.36 to – 0.27, $P < 0.001$) and – 0.34 (95% CI: – 0.4 to – 0.27, $P < 0.001$) of PCOS-related infertility was observed in Asia Pacific (Table 1).

In 2019, China exhibited the highest cases of PCOS-related infertility with 2,133,197 (95% UI: 1,277,929-3,237,032), while Tokelau had the lowest with 3 (95% UI: 2–5) (Fig. 3, Table S1). At the national level, the ASPRs of PCOS-associated infertility ranged from 17.6 per 100,000 people to 585.2 per 100,000 people, Italy exhibited the highest ASPR of PCOS-related infertility, while Albania exhibited the lowest (Fig. 3, Table S1). The ASYRs ranged from 0.1 per 100,000 people to 3.48 per 100,000 people, Italy exhibited the highest, while Albania, Bosnia and Herzegovina, North Macedonia, and Serbia exhibited the lowest. The maximum increase in ASPR was observed in Equatorial Guinea with AAPC of 7.81 (95% CI: 7.68–7.95, $P < 0.001$), and the largest decline was in Northern Mariana Islands with AAPC of – 0.74 (95% CI: – 1.53 – 0.05, $P < 0.001$). The fastest increase in ASYR was observed in Equatorial Guinea with AAPC of 7.8 (95% CI: 7.66–7.95, $P < 0.001$), and the fastest decrease was in Northern Mariana Islands with AAPC of – 0.78 (95% CI: – 1.61 – 0.06, $P < 0.001$) (Fig. 3, Table S1).

Trends of disease burden due to polycystic ovarian syndrome-related infertility by country SDI

Table 1 outlines the number of prevalent cases and YLDs, along with age-standardized rates of prevalence and YLDs attributed to PCOS-related infertility across all SDI regions from 1990 to 2019. In 1990 and 2019, the high-SDI region exhibited the highest ASPR and ASYR of PCOS-related infertility, while the low-SDI region had

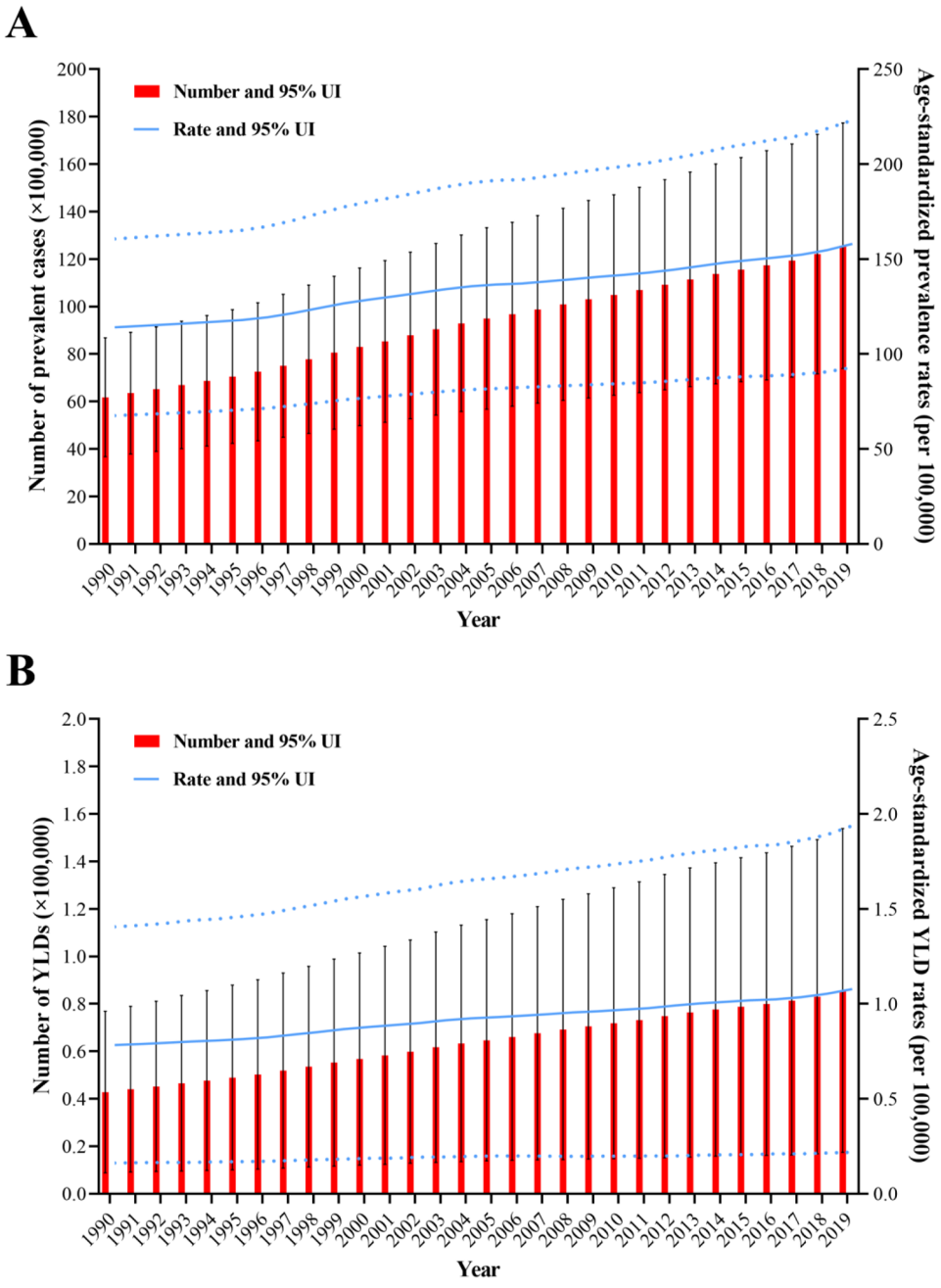

Fig. 1 Global number of prevalent cases and ASPRs (**A**), and number of YLDs and ASYRs from 1990 to 2019. Blue dashed line indicates the upper and lower limits of the 95% uncertainty intervals (95% UIs). ASPR = Age-standardized prevalence rate; ASYR = Age-standardized YLD rate; YLDs = years lived with disability; UI = uncertainty interval

the lowest rates (Table 1). Conversely, the middle-SDI region displayed the highest number of cases and YLDs associated with PCOS-related infertility in both 1990 and 2019. Notably, the low-SDI region experienced the most significant increase in both ASPRs and ASYRs of PCOS-related infertility, with AAPCs of 4.31 (95% CI: 4.26–4.36) and 4.24 (95% CI: 4.18–4.3), respectively (Fig. 4; Table 1). Our analysis also shed light on the connection between sociodemographic changes and the prevalence, as well as YLDs of PCOS-related infertility (Fig. 4). Linear regression analysis demonstrated a positive correlation between ASPRs and ASYRs with SDI ($R = 0.419$ and 0.433, respectively, all $P < 0.0001$). Furthermore, we observed a negative correlation between AAPCs in ASPRs and ASYRs with SDI ($R = -0.570$ and -0.571, respectively, all $P < 0.0001$).

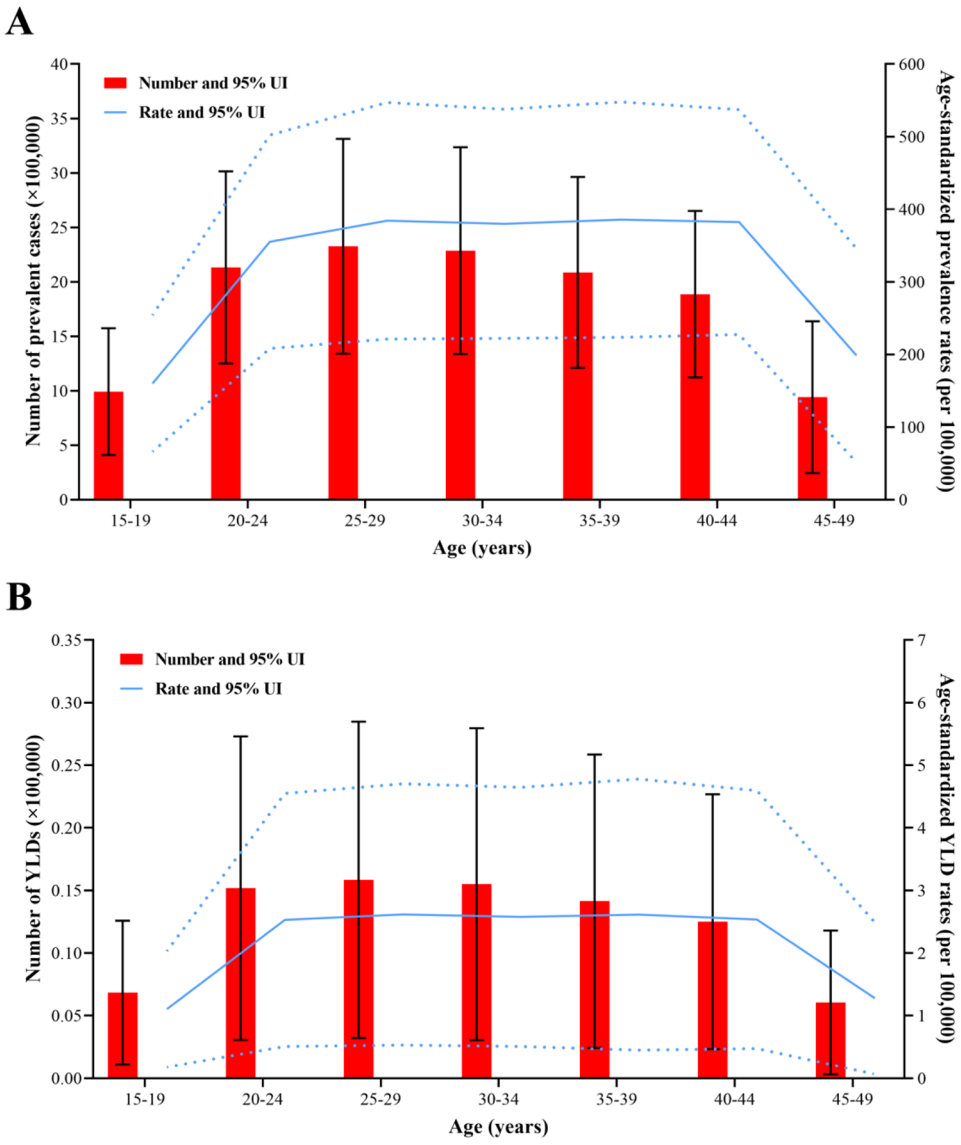

Fig. 2 Global number of prevalent cases and ASPRs (**A**), and number of YLDs and ASYRs by age in 2019. Blue dashed line indicates the upper and lower limits of the 95% uncertainty intervals (95% UIs). ASPR = Age-standardized prevalence rate; ASYR = Age-standardized YLD rate; YLDs = years lived with disability; UI = uncertainty interval

Inequalities in the distribution of polycystic ovarian syndrome-related infertility burdens were quantified by slope index of inequality and the relative concentration index

>Our observations revealed both absolute and relative inequalities associated with SDI, with countries of higher SDI bearing a disproportionately greater burden (Fig. 5, Table S2). From 1990 to 2021, the SII for prevalent cases and YLDs of PCOS-related infertility showed a worsening inequality trend among higher SDI countries, increasing from 121.94 (95% CI: 94.66–149.23) and 0.75 (95% CI: 0.55–0.85) to 146.56 (95% CI: 110.27–182.86) and 0.91 (95% CI: 0.71–1.03), respectively. In contrast, the concentration index for prevalent cases and YLDs of PCOS-related infertility shifted from −0.21 (95% CI: −0.32 to −0.10) and −0.21 (95% CI: −0.31 to −0.09) to −0.17 (95% CI: −0.28 to −0.09) and −0.18 (95% CI: −0.27 to −0.11) (Fig. 5, Table S2).

Discussion

The present study provided a comprehensive assessment of the PCOS-related infertility burden across 204 countries and territories utilizing GBD 2019 data from 1990 to 2019. In this study, we detailed the number of PCOS-related infertility cases, YLDs, ASPRs, and ASYRs, revealing disparities by age, region, nation, and socioeconomics. Our findings revealed that the prevalence, and YLDs of PCOS-related infertility were increasing

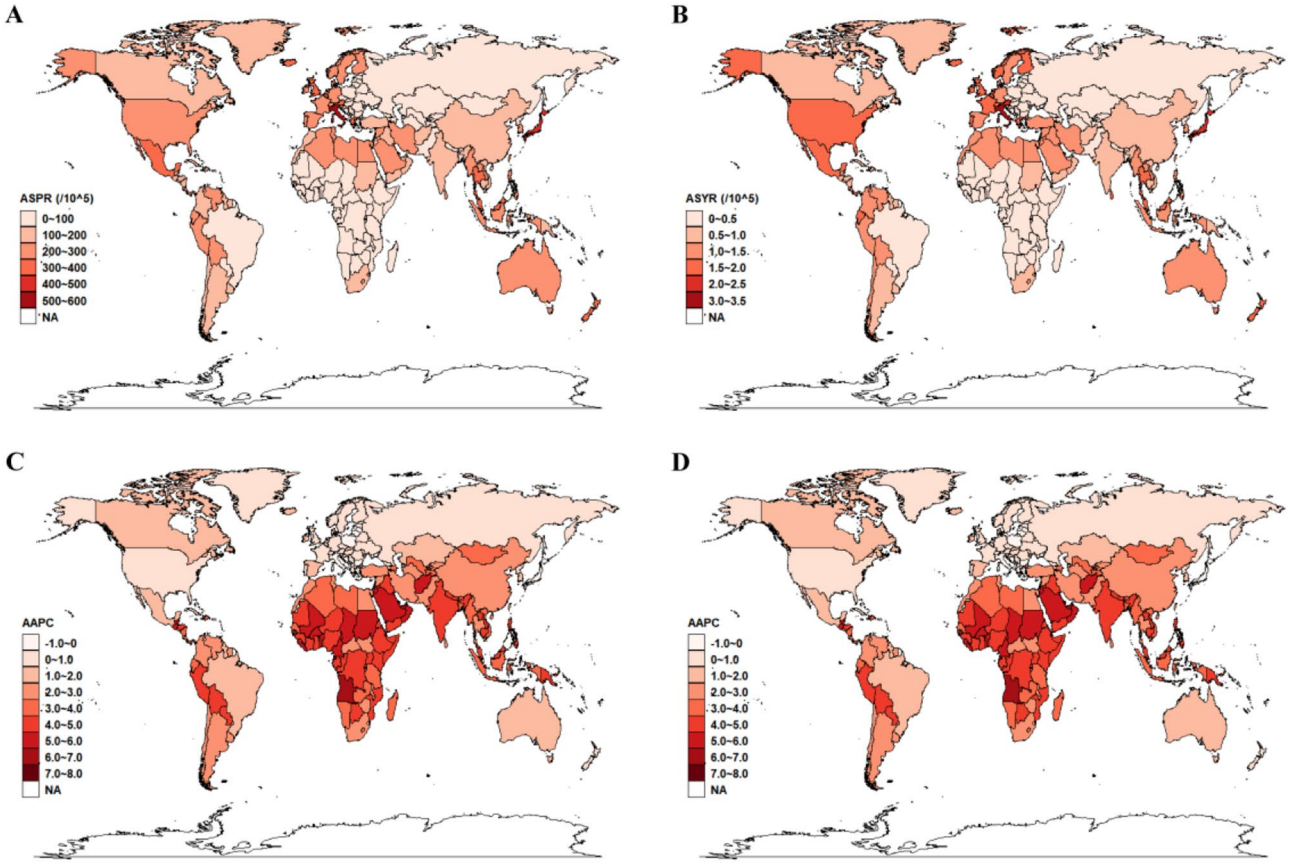

Fig. 3 Global maps of ASPRs (**A**) and ASYRs (**B**) in 2019 as well as AAPC in ASPRs (**C**) and ASYRs (**D**) from 1990 to 2019. ASPR = Age-standardized prevalence rate; ASYR = Age-standardized YLD rate; YLDs = years lived with disability; UI = uncertainty interval

globally. The number of prevalent cases and rate of PCOS peaked in the 25–29 years. Populations with high SDI had the highest ASPRs and ASYRs of PCOS-related infertility, while populations with low SDI exhibited more pronounced upward trends. Despite the presence of clinical practice guidelines and established knowledge designed to ease the challenges associated with PCOS-related infertility, it is clear that the enduringly burdensome nature of this condition requires increased awareness on a global scale.

United Nations Department of Economic Social Affairs (UNDESA) stated that globally, 83 of 201 countries are experiencing an increase in low fertility [18]. According to Sobotka et al., birth rates decreased range from 5.1 to 8.9% compared with the corresponding months of the previous year in seventeen countries spanning Europe, Asia, and the United States [19]. This situation may be exacerbated by infertility, resulting in ultra-low fertility, rapid population aging, and stagnation. A recent report by the World Health Organization estimates that infertility affects approximately 17.5% of adults [20]. PCOS is the most common cause of anovulation and the leading cause of infertility [21]. In the present study, PCOS-related infertility accounted for 12,131,849 prevalent cases and 69,694 YLDs in 2019. The number of cases of infertility associated with PCOS increased 102.28% compared to 1990. This growth is noteworthy, particularly in light of the fact that the global population has increased by a mere 46% over the same period. Since 1990, the ASPR and ASYR rates for PCOS-related infertility have increased by 38.41% and 37.50%, respectively. Although numerous treatments are available for PCOS-related infertility. These include ovulation induction (Letrozole is the first-line agent), gonadotropin, laparoscopic ovarian drilling, and in-vitro fertilization (IVF) [7]. While letrozole has been shown to increase ovulation rates, there remains controversy regarding its impact on pregnancy outcomes and live birth rate, especially among patients with PCOS [22–24]. IVF as a third-line option for women with PCOS-related infertility has been widely applied globally. However, concerns regarding the health of children born through assisted reproductive technology continue to persist [25]. The situation remains less than optimistic despite international efforts to address PCOS-related infertility and associated issues. There is a need for further attention to this related health condition.

The current study discovered that the rude prevalence rate of PCOS-related infertility was highest in the 25–29

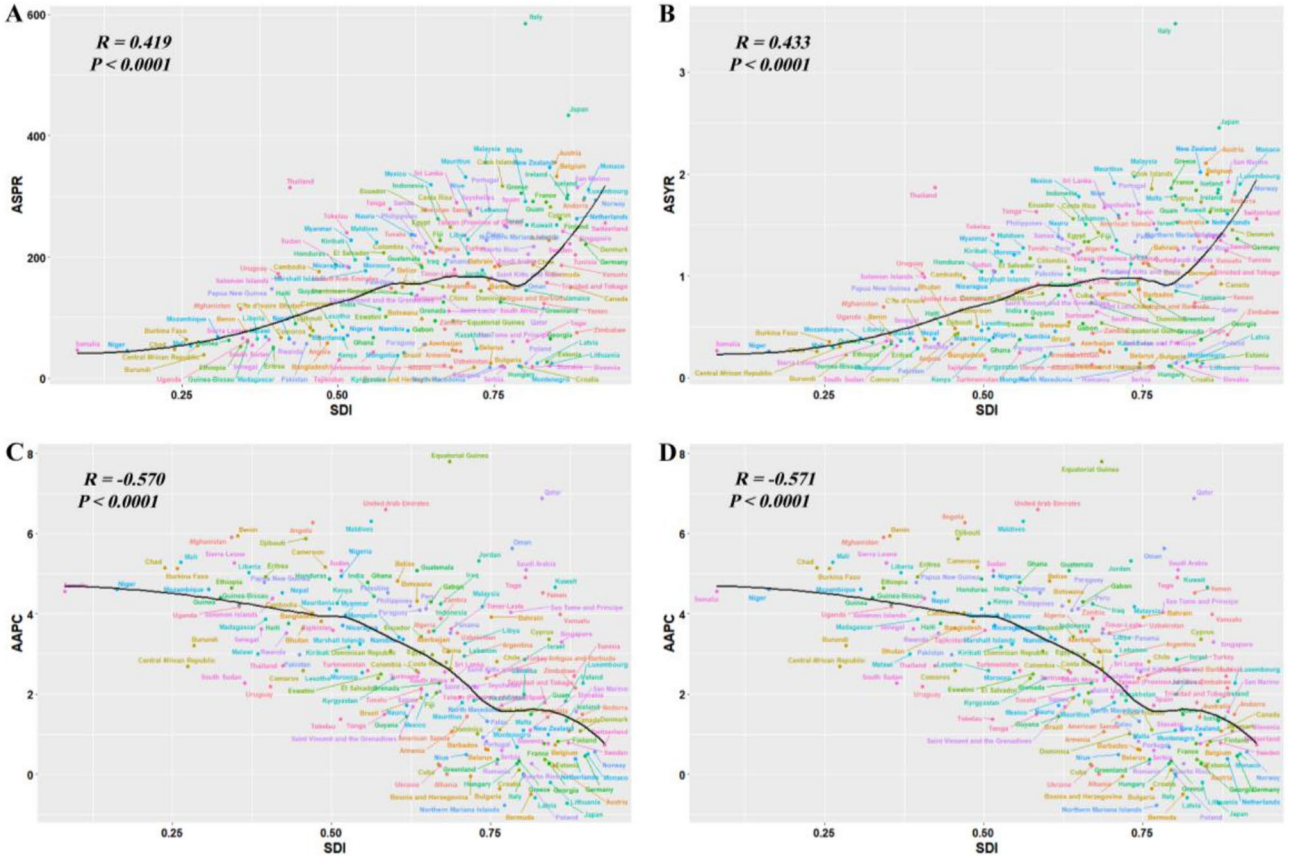

Fig. 4 ASPRs (**A**) and ASYRs (**B**) by SDI for 204 countries and territories in 2019, and AAPC in ASPRs (**C**) and ASYRs (**D**) by SDI for 204 countries and territories from 1990 to 2019. The black line represents the expected values based on ASPRs, ASYRs, AAPC in ASPRs and ASYRs, and SDI in all locations. ASPR = Age-standardized prevalence rate; ASYR = Age-standardized YLD rate; YLDs = years lived with disability; SDI = socio-demographic index

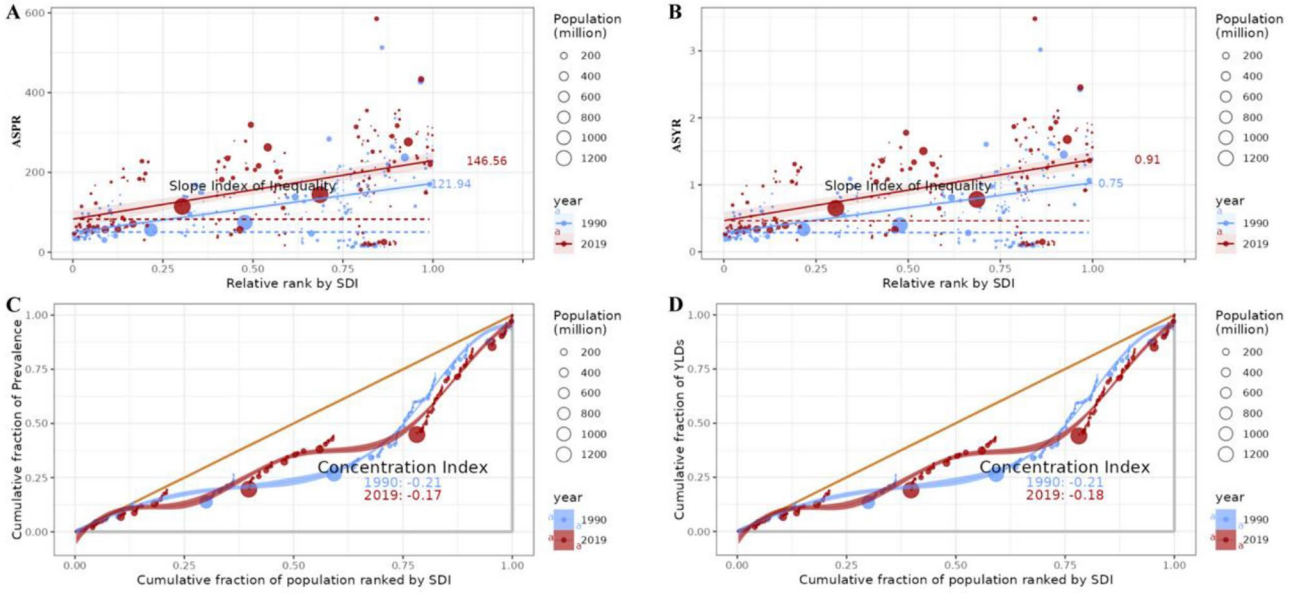

Fig. 5 Health inequality regression curves (**A**, **B**) and concentration curves (**C**, **D**) for the prevalence and YLDs of Polycystic Ovarian Syndrome-Related Infertility worldwide, 1990 and 2019. ASPR = Age-standardized prevalence rate; ASYR = Age-standardized YLD rate; YLDs = years lived with disability; SDI = socio-demographic index

age, highlighting the need to strengthen prevention and control efforts targeting this age group. Deulle M et al. found that the group diagnosed with PCOS is more likely to prepare for pregnancy and promote healthy behavior to alleviate PCOS than those without PCOS [26], indicating the importance of visiting doctors regularly and increasing awareness of health beliefs and knowledge of PCOS to young women. Additionally, personalized lifestyle guidance including dietary improvement, moderate exercise, and stress management would contribute positively to PCOS prevention and treatment [27]. Although the crude prevalence and YLD number were at a lower level in women 15–19 years of age, the group of people still deserves attention. Because of PCOS in adolescent females can present difficulties in diagnosis due to the fact that initial PCOS symptoms, such as acne, menstrual irregularity, and polycystic ovary morphology, may appear to be typical developmental changes that occur during puberty [28]. Therefore, more attention should be directed towards young women of reproductive age, especially in the age groups of 25–29 and 15–19, encompassing aspects such as health check-ups and promotion of healthcare knowledge.

The prevalence and YLDs of PCOS-related infertility varied considerably between regions and countries. East Asia had the most prevalent cases and YLDs of PCOS-related infertility in 2019. As China has a vast population base, its high case number and YLDs are intimately related. Since the 1990s, China has seen numerous significant social and economic transformations, as well as changes in people's lives, in tandem with the rapidly growing incidence of obesity [29]. In China, by 2030, the prevalence of overweight (BMI 24.0–28.0 kg/m^2) and obesity (BMI ≥ 28·0 kg/m^2) might reach 65.3% in adults [29]. On the other hand, exposure to endocrine-disrupting chemicals (EDCs) may have a negative impact on the hormonal system [30]. Meanwhile, we found that Asia Pacific like Japan and the Northern Mariana Islands, have the fastest decrease in ASPR of PCOS-related infertility, owing in part to the dietary structure, given that both areas are situated in the Pacific Ocean, which may have an impact on obesity and body mass index [31]. Additionally, the particularly fast-increasing trends in Western Sub-Saharan Africa. A previous study has reported that Africa exhibits a significantly elevated incidence of infertility, which presents a paradoxical situation given the concurrent accelerated growth of its population [2].

The highest incidence of cases and YLDs was noted in middle SDI regions, primarily due to the significant populations of China and India classified within this category. Furthermore, advancements in medical care have facilitated the widespread adoption of high-quality ultrasound equipment and an increasing rate of PCOS diagnoses in middle SDI countries over the past three decades. This study also demonstrates a positive correlation between ASPRs and ASYRs with the SDI, indicating that developed regions tend to report higher PCOS-related infertility. The prevalence of Westernized diets in developed nations, which is associated with increased risks of obesity, insulin resistance, and metabolic disorders—all of which are linked to PCOS—likely contributes to this potentially causal relationship between SDI and PCOS-related infertility. Moreover, developed areas benefit from higher levels of medical technology, widespread health education, and a strong emphasis on women's health, which collectively result in relatively higher disease rates that reflect increased attention to these health issues. In contrast, low SDI regions exhibit lower ASPRs and ASYRs, which may be attributed to inadequate healthcare resources and limited diagnostic capabilities [32]. Cultural and societal beliefs in some low SDI regions can also influence attitudes toward the diagnosis and treatment of infertility [2, 32], resulting in a lower patient willingness to seek medical assistance. Consequently, accurate data on the disease burden of low-SDI regions remains elusive. However, these low-development areas exhibit rising trends in AAPCs due to inadequate public health services, lower treatment levels, and insufficient emphasis on women's health. This situation not only reflects the unequal distribution of medical resources but also reveals significant shortcomings in disease prevention and health education in these regions. Therefore, there is an urgent need to pay more attention to women in low-development areas and to invest additional resources to improve their health status, thereby effectively narrowing health disparities between different levels of development. Developing countries should learn from the experiences of developed nations to emphasize the significance of PCOS in healthcare policy formulation, particularly by increasing financial allocations aimed at reducing the societal burden of PCOS-related infertility.

While the presented results are accurate, they may not provide optimal comparability for evaluating and tracking inequality. Consequently, we calculated the SII and the concentration index based on SDI to enhance comparability. Between 1990 and 2019, the overall burden of PCOS-related infertility has risen, with a modest reduction in distributional inequality. This suggests that, relative to low-SDI regions, countries with higher SDI face a worsening inequality in burden. Nevertheless, the gradual decrease in the concentration index over time indicates a narrowing of this inequality, potentially attributable to improved healthcare access, greater global awareness of PCOS, and advancements in reproductive healthcare in lower-SDI regions. Despite these positive shifts, persistent disparities highlight the need for targeted interventions in lower-income areas, where

women may have restricted access to specialized care for PCOS-related infertility. In summary, while some progress has been achieved, substantial inequalities remain in the global distribution of the PCOS-related infertility burden. Addressing these disparities is essential to ensure equitable healthcare access and to mitigate the global impact of PCOS.

Limitations

This study has several limitations that necessitate careful consideration. Firstly, the availability and quality of data related to PCOS-induced infertility are constrained, particularly in developing countries, potentially introducing bias into the model estimates. To refine the precision of future evaluations, further research is imperative to investigate methods for mitigating data bias. Secondly, women experiencing PCOS-related infertility, especially in developing regions, may not actively seek medical care, resulting in their underrepresentation in our analysis and potentially leading to an underestimation of the global burden of PCOS-related infertility. Thirdly, a significant time gap existed between data collection and inclusion in the database, potentially impacting the timeliness of the assessments of PCOS-related infertility. As the Global Burden of Disease (GBD) study advances, it is vital to explore and compile more comprehensive information on PCOS-induced infertility to enhance our understanding of this critical public health concern. Addressing these limitations is crucial for facilitating more accurate and current assessments, ultimately contributing to the improvement of preventive measures and healthcare planning for PCOS-related infertility.

Conclusions

In summary, our research highlights a worrisome increase in the prevalence and YLDs associated with PCOS-related infertility. Disparities across age groups, socio-economic status, regions, and nations underscore the pressing need for heightened global awareness regarding the enduringly burdensome nature of PCOS-related infertility. This study offers a comprehensive insight into the global landscape of PCOS-related infertility, emphasizing the necessity for increased awareness, targeted interventions, and further research to address the multifaceted challenges posed by this impactful condition. It is crucial for initiatives to extend beyond medical interventions, encompassing the promotion of healthy behaviors, regular healthcare visits, and personalized lifestyle guidance to effectively mitigate the escalating burden of PCOS-related infertility on a global scale.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-024-03537-7.

Supplementary Material 1

Acknowledgements
We would like to thank the Institute for Health Metrics and Evaluation staff and its collaborators who prepared these publicly available data.

Author contributions
Conception and design: MH, YXW, XBY, XHZ. Acquisition of data: XBY. Analysis and interpretation of data: XBY. Drafting the manuscript: MH and YXW. Critical revision of the manuscript: YY and XHZ. Final approval to be published: all authors.

Funding
This work was supported by the Natural Science Foundation of China (81960273); the Gansu Natural Science Foundation (21JR1R097); and the Intra-Hospital Fund of the First Hospital of Lanzhou University (ldyyyn2021-82).

Data availability
The data used for these analyses are all publicly available at http://ghdx.healthdata.org/gbd-results-tool.

Declarations

Ethics approval and consent to participate
This study was based on publicly available, de-identified data from the Global Burden of Disease Study 2019. No ethical approval was required, as the data are anonymized and do not contain any personally identifiable information.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Reproductive Medicine Center, The First Hospital of Lanzhou University, Lanzhou City, Gansu 730000, China
[2]Key Laboratory for Reproductive Medicine and Embryo, Lanzhou City, Gansu 730000, China
[3]The First people's Hospital of Lanzhou City, Lanzhou City, Gansu 730000, China

Received: 3 September 2024 / Accepted: 26 December 2024
Published online: 23 January 2025

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