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Emerging trends and cross-country health inequalities in congenital birth defects: insights from the GBD 2021 study

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Abstract

Background Previous studies predominantly focused on single types of congenital birth defects (CBDs) or specific national prevalence. This study adopts a holistic perspective to assess current trends and health inequalities in birth incidence rate of various types of CBDs, providing novel insights to inform public health policy formulation.

Methods Global, socio-demographic index (SDI) regional, and country-specific estimates incidence cases and rate at birth of CBDs from 1990 to 2021 were derived from the Global Burden of Disease (GBD) 2021. Joinpoint analysis and autoregressive integrated moving average predictive models were employed to evaluate temporal trends in the birth incidence rate of CBDs for the period 2022–2031. Additionally, analysis of associations and health inequalities were conducted to examine the relationship between SDI and the birth incidence rate of CBDs across countries.

Results Globally, the birth incidence rate decreased from 5811.17/100k population in 1990 to 5563.72/100k population in 2021, with low SDI regions recording the lowest rate and cases. Joinpoint analysis revealed a global decrease in the birth incidence rate of CBDs (average annual percentage change, AAPC: -0.14%, 95%*CI*: -0.15% to -0.12%). The most significant decline was observed in neural tube defects (NTD) (AAPC: -1.35%, 95%*CI*: -1.42% to -1.28%). However, only birth incidence rate of orofacial clefts (OC) is projected to decrease globally the next decade. Within the five SDI regions, the birth incidence rate of OC is also projected to decrease probably. The analysis revealed negative correlations between congenital heart anomalies (CHA), NTD, and SDI, with NTD showing both absolute and relative health inequalities.

Conclusions Despite the general decline in overall birth incidence rate of CBDs, projections suggested a probable increasing trend for all types except OC. This underscores the necessity for enhanced surveillance and intervention measures. Furthermore, the successful prevention policies implemented for NTD could serve as effective models for addressing other types of CBDs, thereby improving the current global situation of CBDs.

Keywords Congenital birth defects, GBD, Incidence, Trend, Prediction, Health inequality

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Introduction

Congenital birth defects (CBDs) encompass structural or functional abnormalities that arise during the embryonic or fetal stages, significantly impacting physical or intellectual development [1, 2]. Annually, approximately 8 million infants are born with CBDs worldwide, and deaths due to CBDs contribute to about 10% of neonatal deaths [3, 4]. Although advancements in diagnosis, treatment, and care have alleviated some fatal birth defects, survivors often face potential social discrimination and long-term complications, necessitating ongoing medical support throughout their lives [5–7]. For example, children with congenital heart anomalies (CHA) have an increasing risk of developing chronic heart failure and acquiring cardiovascular diseases in the future. Consequently, CBDs impose a substantial burden on affected individuals and their families [8, 9].

CBDs result from genetic and environmental factors and represented a significant health burden that can be mitigated through effective intervention strategies. Maternal folic acid supplementation during the periconceptional period, for example, can prevent neural tube defects (NTD) in offspring [10]. Establishing robust medical surveillance systems to accurately identify CBDs was crucial for implementing targeted interventions to alleviate the burden. However, socioeconomic disparities hinder the development of comprehensive CBDs surveillance systems in many developing countries [11, 12]. Consequently, many intervention measures were inadequately implemented, making it challenging to control the incidence of CBDs. While developed countries have seen a significant reduction in the burden of CBDs, approximately 94% of severe cases occur in low- and middle-income countries [13]. Monitoring the incidence of CBDs across regions and countries and comparing differences is essential for adjusting relevant policies effectively.

Current research on the Global Burden of Disease (GBD) related to CBDs has focused on single types, without conducting in-depth analyses across different types of CBDs [2, 14]. Additionally, the scope of such studies tends to be limited, covering specific countries or territories and lacking a comprehensive global perspective [15]. This study provides a detailed evaluation of the distribution of CBDs by leveraging birth incidence cases and rate from various types, aiming to optimize the allocation of healthcare resources and to inform the development of public health strategies for monitoring and preventing these defects. The GBD 2021 offers new data on the incidence at birth of CBDs worldwide, providing a comprehensive perspective on the epidemiological magnitude of these defects. This study adopts a holistic view to assess current epidemiological trends and various types of CBDs, thereby offering novel insights to inform public health policy formulation. Reevaluating and predicting trends in the birth incidence rate of CBDs at global, SDI regional, and national levels, along with assessing health inequalities between countries, is crucial for achieving a global consensus on preventing CBDs, fostering international health cooperation, and advancing the United Nations' Sustainable Development Goals.

Methods

Data sources

This study utilized data from GBD 2021 (https://vizhub.healthdata.org/gbd-results/). In the GBD database, CBDs were diagnosed according to the International Classification of Diseases, 10th Revision, specifically within the coding range Q00-Q99. More details were available in S1 table. The data sources included literature reports, multiple international birth defect registries, surveillance systems, inpatient hospital data and MarketScan claims data [16]. These defects included various types such as CHA, congenital musculoskeletal and limb anomalies (CMLA), urogenital congenital anomalies (UCA), digestive congenital anomalies (DCA), orofacial clefts (OC), Down syndrome, NTD, Turner syndrome, Klinefelter syndrome, and other chromosomal abnormalities. For this study, data on Down syndrome, Turner syndrome, Klinefelter syndrome, and other chromosomal abnormalities were consolidated into a single group for subsequent analysis (Total chromosomal congenital birth defects, TCCBD) [16]. Given the unique onset timing of CBDs, the GBD2021 database recalculated the incidence rate at birth. Birth incidence cases and rate were reported in the form of point estimate and 95% uncertainty intervals (UI). The 95% uncertainty intervals (UI) in the GBD study were produced based on the 25th and 975th ordered values of 1000 random draws of the posterior distribution. The models and estimation processes for this indicator were detailed in other publications [16]. This study proceeds with further analysis based on this recalculated indicator.

The GBD 2021 provided specific SDI values for 204 countries and territories and categorized them into 5 categories based on the socio-demographic index (SDI), reflecting epidemiological similarity. The SDI classifications are: High SDI, High-middle SDI, Middle SDI, Low-middle SDI, and Low SDI. The values of these quintile can be found on the aforementioned website. The SDI was a composite indicator reflecting the social and economic conditions that impact health in each country and region, including per capita income, average educational attainment for the population aged 15 and over, and fertility rate for women under 25 [16].

Statistical analysis

Joinpoint regression model (JRM) was employed to assess the temporal trends of CBDs and each type in global and SDI regions over the period 1990–2021. Joinpoint Software (version 4.8.0.1; National Cancer Institute, Rockville, MD, USA) was used to systematically evaluate these trends and determine the statistical significance of changes at connection points. The annual percentage change (APC) and average annual percentage change (AAPC) were calculated to quantify the direction and magnitude of trends. Based on this, the Autoregressive Integrated Moving Average(ARIMA) model was applied to predict future trends in the incidence rate at birth of CBDs from 2022 to 2031. The ARIMA model, a combination of autoregressive and moving average models, is widely used for forecasting disease trends due to its efficacy. The Ljung-Box test was used to evaluate the model's fit, with $p > 0.05$ indicating a good fit. Prediction accuracy was assessed using root mean square error (RMSE), mean absolute error (MAE), and mean absolute percentage error (MAPE), with lower values indicating higher precision.

To analyze association, spearman correlation and locally weighted linear regression model were used to examine the relationship between the birth incidence rate of CBDs and each type and SDI. Further analysis of health inequality in the birth incidence rate of CBDs and each type was conducted using the slope index of inequality and the concentration index, as recommended by the WHO in the Health Inequality Monitoring Manual. Slope index of inequality was calculated by regressing the birth incidence rate of CBDs and each type on a relative SDI scale related to income, representing the absolute difference in a health measure between a subgroup with the highest level of education or wealth and a subgroup with the lowest. The concentration index was obtained by fitting the Lorenz curve to the cumulative distribution of the population ranked by SDI and the cumulative fraction for the birth incidence rate of CBDs and each type. Integrating the area under the curve indicates the degree to which a health indicator is concentrated in a disadvantaged or advantaged group [17]. Repeated iterative weighted linear regression was used to account for heteroscedasticity. A positive value indicates higher birth incidence rate in subgroups with higher SDI, whereas a negative value indicates higher birth incidence rate in subgroups with lower SDI. The greater the absolute value, the greater the inequality. ARIMA forecasts, association analysis, and health inequality analysis were performed using R software (version 4.3.1) and Stata/MP 16.0 (StataCorp, College Station, TX), with $p < 0.05$ considered statistically significant.

Result

The birth incidence cases and rate of CBDs and its types

Globally, the birth incident cases of CBDs decreased from 7658372.57 (95%*UI*: 6649818.93 to 8882947.09)in 1990 to 7198542.23 (95%*UI*: 6203686.76 to 8356382.81)in 2021. Correspondingly, the birth incidence rate decreased from 5811.17/100k population (95%*UI*: 5045.88 to 6740.38) in 1990 to 5563.72/100k population (95%*UI*: 4794.80 to 6458.61) in 2021. Among the five SDI regions, Low SDI region recorded the lowest birth incidence rate and cases, as depicted in Table 1 and S2 Table.

At the country level, the top five countries with the highest birth incidence rate of CBDs in 2021 were the Central African Republic, Tajikistan, Brunei Darussalam, Turkmenistan, and Haiti. The countries with the highest cases of CBDs were India, China, Nigeria, Pakistan, and Indonesia. There was considerable overlap with the top five countries in birth incidence rate and cases in 1990. Detailed data for other countries and types of CBDs were showed in S3 Table.

Temporal trend and projection in the birth incidence rate of CBDs and its types

Joinpoint analysis revealed that the global birth incidence rate of CBDs declined during 1990–2021 (AAPC: -0.14%,95%*CI*: -0.15% to -0.12%, $p < 0.001$). The most significant decline was observed in NTD (AAPC: -1.35%,95%*CI*: -1.42% to -1.28%, $p < 0.001$).

Overall, the birth incidence rate of CBDs declined in all SDI regions, with the most substantial decrease observed in the middle SDI region (AAPC: -0.33%,95%*CI*: -0.35% to -0.31%, $p < 0.001$). Specific types of CBDs such as CHA, NTD, OC, UCA, and TCCBD saw the most significant declines in the high-middle SDI regions. In contrast, CMLA decreased most in the middle SDI region, while DCA showed the greatest decline in the low SDI region. Among all types and regions, the high-middle SDI region for NTD exhibited the largest decrease (AAPC: -2.74%,95%*CI*: -2.86% to -2.61%, $p < 0.001$). However, it was noteworthy that UCA displayed an upward trend globally and across all five SDI regions during 2016–2021. The high SDI region experienced the highest increase in birth incidence rate of UCA during this period (AAPC: 5.59%, 95%*CI*:4.13 to 7.07%, $p < 0.001$). More details are shown in Fig. 1 and S4 Table.

The ARIMA model was used to forecast the birth incidence rate of CBDs and its types globally and across five SDI regions for the period 2022–2031. The residuals of all models passed the Ljung-Box test, indicating a good fit (Fig. 2 and S5 Table). The projected birth incidence rate of CBDs and its types from 2022 to 2031 are detailed in the table. Globally, the birth incidence rate of CBDs was expected to decrease from 5551.95 /100k population (95%*CI*: 5542.9 to 5561.0) in 2022 to 5446.00 /100k

Table 1 Incidence cases and rate of congenital birth defects and its types in global and five SDI regions in 2021

Cause	Metric	Location					
		Global	High SDI	High-middle SDI	Middle SDI	Low-middle SDI	Low SDI
All congenital birth defects	Cases (95%UI)	7198542.23 (6203686.76,8356382.81)	463766.79 (408437.78,526524.21)	612106.94 (528249.77,712739.78)	1585096.34 (1364385.12,1846742.85)	2212700.38 (1903046.10,2565788.23)	2319368.90 (1982333.52,2711204.42)
	Rate (95%UI)	5563.72 (4794.8,6458.61)	4538.02 (3996.62,5152.11)	5267.33 (4545.72,6133.31)	4966.74 (4275.16,5786.58)	5628.84 (4841.11,6527.05)	6404.51 (5473.85,7486.49)
Congenital heart anomalies	Cases (95%UI)	2300327.37 (1813141.51,2967225.21)	121555.97 (101071.61,148799.17)	163179.06 (128947.33,211230.84)	514055.50 (395379.86,679956.28)	734834.13 (581389.55,956066.37)	764998.77 (602681.04,990462.11)
	Rate (95%UI)	1777.91 (1401.37,2293.36)	1189.44 (989.00,1456.02)	1404.20 (1109.62,1817.69)	1610.74 (1238.88,2130.57)	1869.33 (1478.98,2432.11)	2112.40 (1664.19,2734.98)
Congenital musculoskeletal and limb anomalies	Cases (95%UI)	2437890.12 (1737729.85,3355568.45)	171897.72 (126645.61,233055.44)	252078.40 (183567.72,346342.25)	530552.20 (377547.35,749651.36)	709077.11 (500010.8,978014.08)	772304.97 (535641.71,1080797.35)
	Rate (95%UI)	1884.23 (1343.08,2593.50)	1682.04 (1239.24,2280.48)	2169.20 (1579.65,2980.36)	1662.43 (1183.01,2348.96)	1803.80 (1271.97,2487.95)	2132.58 (1479.08,2984.42)
Digestive congenital anomalies	Cases (95%UI)	459018.32 (364141.41,585158.36)	35920.54 (29318.02,43068.87)	47342.58 (37951.5,58046.19)	120978.56 (96244.74,151492.69)	131803.98 (102661.03,174378.85)	122596.02 (95338.56,159854.83)
	Rate (95%UI)	354.77 (281.44,452.27)	351.49 (286.88,421.43)	407.39 (326.58,499.50)	379.07 (301.57,474.69)	335.29 (261.16,443.60)	338.53 (263.26,441.41)
Neural tube defects	Cases (95%UI)	120932.04 (106318.25,135884.36)	3504.53 (3141.23,3855.15)	5027.73 (4492.97,5519.23)	15947.18 (13979.77,17938.65)	31990.74 (27889.8,36209.70)	64365.69 (56467.04,72678.91)
	Rate (95%UI)	93.47 (82.17,105.02)	34.29 (30.74,37.72)	43.26 (38.66,47.49)	49.97 (43.80,56.21)	81.38 (70.95,92.11)	177.73 (155.92,200.69)
Orofacial clefts	Cases (95%UI)	183302.41 (135255.43,241690.82)	12250.69 (8958.26,15793.47)	14891.05 (10856.42,19103.22)	41628.60 (30595.38,54118.79)	61922.27 (45962.81,82936.30)	52492.49 (37730.85,70330.42)
	Rate (95%UI)	141.67 (104.54,186.80)	119.87 (87.66,154.54)	128.14 (93.42,164.39)	130.44 (95.87,169.58)	157.52 (116.92,210.98)	144.95 (104.19,194.20)
Total chromosomal congenital birth defects	Cases (95%UI)	602835.51 (488968.11,740099.08)	47402.40 (40292.08,56498.18)	47068.22 (39490.21,56110.14)	123905.29 (101973.25,150842.95)	183420.57 (147476.58,227810.14)	200537.84 (160275.27,251573.87)
	Rate (95%UI)	465.93 (377.92,572.02)	463.84 (394.26,552.84)	405.03 (339.82,482.84)	388.24 (319.52,472.65)	466.60 (375.16,579.52)	553.75 (442.57,694.67)
Urogenital congenital anomalies	Cases (95%UI)	1094236.46 (823142.89,1438204.65)	71234.94 (54781.65,91380.47)	82519.88 (62047.78,108329.13)	238029.00 (176352.12,314090.61)	359651.58 (268523.42,481249.54)	342073.11 (256408.48,453935.80)
	Rate (95%UI)	845.73 (636.2,1111.58)	697.04 (536.05,894.17)	710.10 (533.94,932.2)	745.84 (552.58,984.17)	914.91 (683.09,1224.24)	944.57 (708.02,1253.46)

Note: SDI: Socio-Demographic Index; UI: uncertain interval

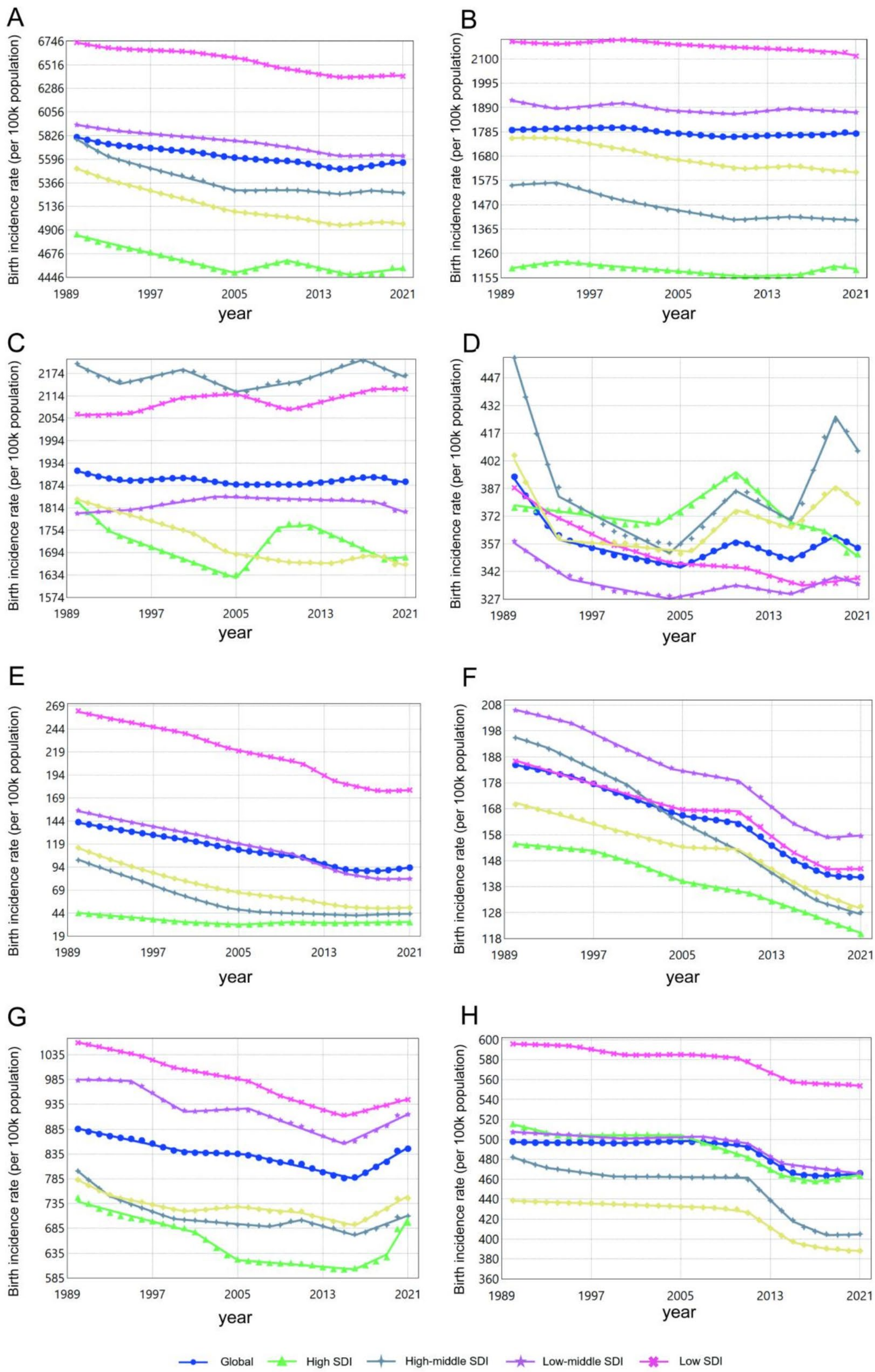

Fig. 1 Joinpoint analysis on birth incidence rate for CBDs and its types from 1990 to 2019. Note: **A**: Congenital birth defects, **B**: Congenital heart anomalies, **C**: Congenital musculoskeletal and limb anomalies, **D**: Digestive congenital anomalies, **E**: Neural tube defects, **F**: Orofacial clefts, **G**: Urogenital congenital anomalies, **H**: Total chromosomal congenital birth defects, SDI: Socio-Demographic Index

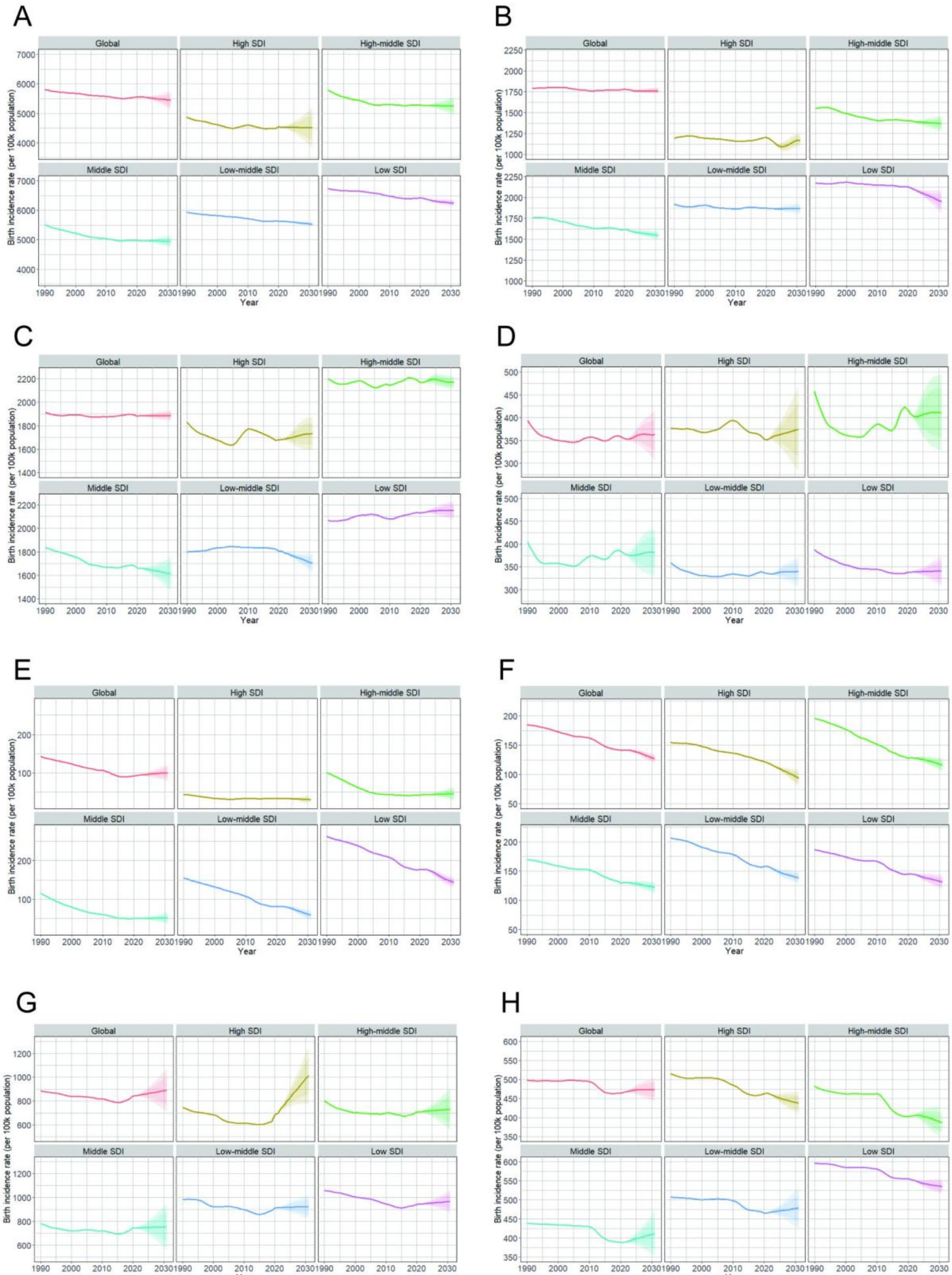

Fig. 2 Birth incidence rate of CBDs and its types from 1990 through 2032 forecasts. Note: **A**: Congenital birth defects, **B**: Congenital heart anomalies, **C**: Congenital musculoskeletal and limb anomalies, **D**: Digestive congenital anomalies, **E**: Neural tube defects, **F**: Orofacial clefts, **G**: Urogenital congenital anomalies, **H**: Total chromosomal congenital birth defects, SDI: Socio-Demographic Index

population (95%*CI*: 5139.23 to 5752.77) in 2031. The five SDI regions also exhibited a downward trend, with the most significant decline observed in the low SDI region (from 6379.08 /100k population (95%*CI*: 5456.46 to 5602.09) in 2022 to 6241.31 /per 100k population (95%*CI*: 6132.27 to 6350.34) in 2031).

However, among the various types of CBDs, only the birth incidence rate of OC· were anticipated to decrease globally. In contrast, the birth incidence rate of CHA, CMLA, DCA, NTD and TCCBD were projected to increase globally, with UCA showing the largest rise (from 850.14 in 2022 to 889.86 in 2031). Notably, within all the five SDI regions, the birth incidence rate of UCA was projected to increase, while the birth incidence rate of OC was expected to decline. The high SDI region was forecasted to exhibit the largest increase in UCA and the most substantial decline in OC.

Correlation between the birth incidence rate of CBDs and their types and the SDI

Figure 3 illustrated the relationship between the birth incidence rate of CBDs, its various types, and the SDI across 204 countries in 1990 and 2021. The analysis revealed no association between birth incidence rate excluding DCA and OC in 1990 and excluding OC in 2021 with SDI. In contrast, CBDs and its types exhibited a negative correlation with SDI. In 2021, the negative correlation between the birth incidence rate of CBDs and SDI was stronger (ρ=-0.63, $p<0.001$) compared to 1990 (ρ=-0.59, $p<0.001$). This indicated a greater decline in birth incidence rate of CBDs with increasing SDI in 2021 than in 1990. Notably, the birth incidence rate of CHA and NTD had the highest negative correlation with SDI in both 1990 and 2021. Notably, the birth incidence rate

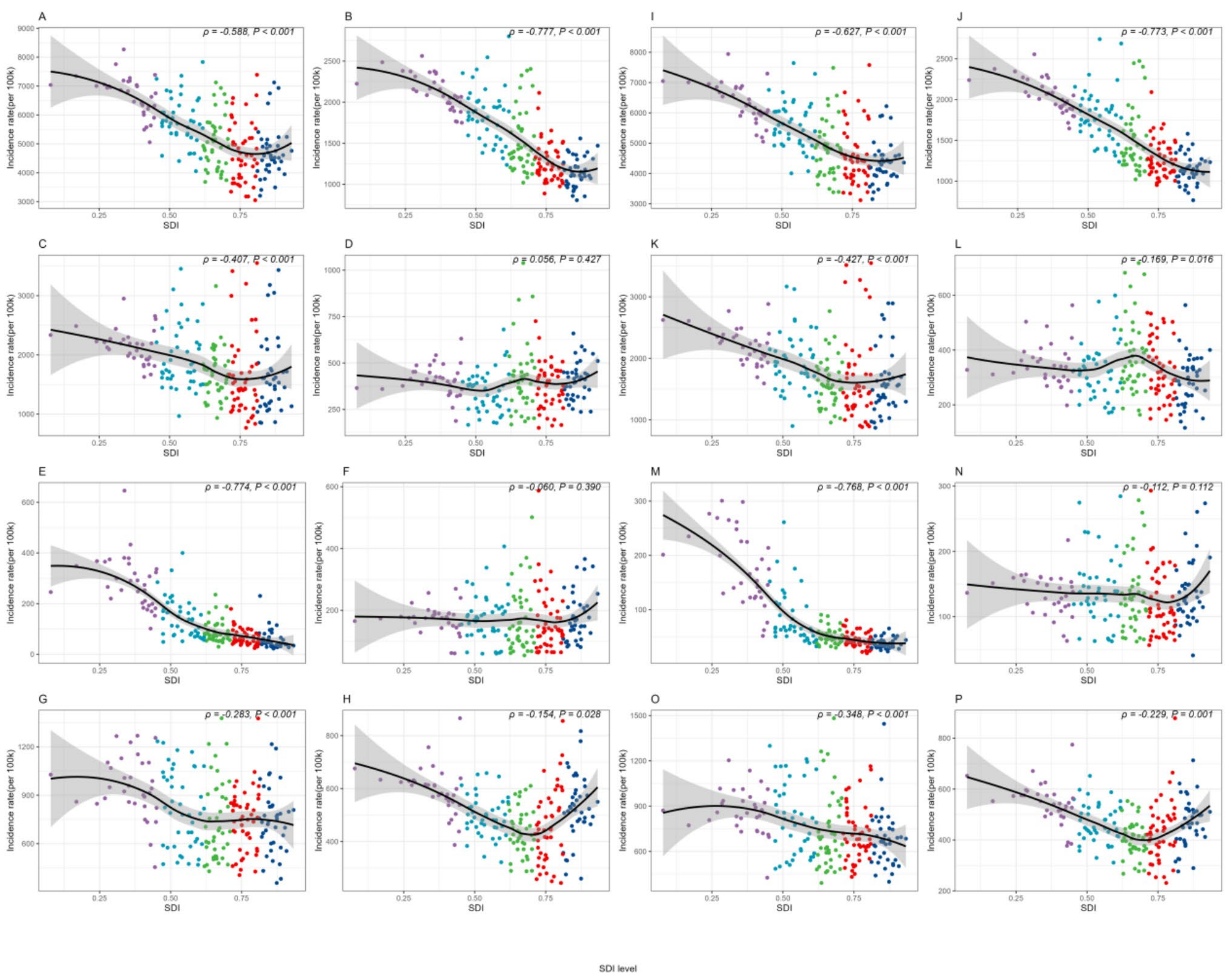

Fig. 3 Association between birth incidence rate of CBDs and its types and SDI in 1990 and 2021. Note: **A**-**H**:1990; I-P:2021; **A** & **I**: Congenital birth defects, **B** & **J**: Congenital heart anomalies, **C** & **K**: Congenital musculoskeletal and limb anomalies, **D** & **L**: Digestive congenital anomalies, **E** & **M**: Neural tube defects, **F** & **N**: Orofacial clefts, **G** & **O**: Urogenital congenital anomalies, **H** & **P**: Total chromosomal congenital birth defects, SDI: Socio-Demographic Index

Table 2 Measures for health inequality in birth incidence rate of congenital birth defects and its types

Cause	Health inequality metrics	Year	Value(95%CI)
Congenital birth defects	Slope index	1990	-2326.01(-2670.58 to -1981.43)
		2021	-2296.16(-2622.67 to -1969.65)
	Concentration index	1990	-0.04(-0.03 to -0.05)
		2021	-0.06(-0.05 to -0.07)
Congenital heart anomalies	Slope index	1990	-984.44(-1109.91 to -858.97)
		2021	-1007.91(-1128.95 to -886.88)
	Concentration index	1990	-0.08(-0.07 to -0.09)
		2021	-0.09(-0.08 to -0.1)
Congenital musculoskeletal and limb anomalies	Slope index	1990	-684.03(-872.31 to -495.74)
		2021	-808.21(-995.22 to -621.19)
	Concentration index	1990	0.01(0.03 to -0.01)
		2021	-0.03(-0.01 to -0.04)
Digestive congenital anomalies	Slope index	1990	-3.27(-50.44 to 43.91)
		2021	-32.09(-78.13 to 13.94)
	Concentration index	1990	0.03(0.05 to 0.01)
		2021	0.03(0.04 to 0.01)
Neural tube defects	Slope index	1990	-212.63(-229.4 to -195.86)
		2021	-117.14(-128.37 to -105.91)
	Concentration index	1990	-0.25(-0.22 to -0.28)
		2021	-0.33(-0.29 to -0.37)
Orofacial clefts	Slope index	1990	-26.63(-56.11 to 2.84)
		2021	-15.75(-35.67 to 4.17)
	Concentration index	1990	-0.04(-0.02 to -0.07)
		2021	-0.04(-0.02 to -0.06)
Urogenital congenital anomalies	Slope index	1990	-240.59(-327.78 to -153.4)
		2021	-203.38(-292.05 to -114.71)
	Concentration index	1990	-0.08(-0.06 to -0.1)
		2021	-0.08(-0.06 to -0.1)
Total chromosomal congenital birth defects	Slope index	1990	-110.80(-156.31 to -65.28)
		2021	-107.85(-148.39 to -67.31)
	Concentration index	1990	-0.03(-0.02 to -0.04)
		2021	-0.06(-0.05 to -0.07)

Note: SDI: Socio-Demographic Index; Slope index: It represents the absolute difference in a health measure between a subgroup with the highest level of education or wealth and a subgroup with the lowest. Concentration index: It indicates the degree to which a health indicator is concentrated in a disadvantaged or advantaged group

of TCCBD displayed an "inverted V" relationship with SDI, initially decreasing and then increasing as SDI rose.

Health inequality in CBDs and its types among 204 countries in 1990 and 2021

At the national level, absolute and relative inequality in the birth incidence rate of CBDs and its types related to the SDI were observed. Table 2 showed that, with the exception of DCA and OC, the birth incidence rate of CBD and its types were disproportionately shouldered by countries with lower SDI. As indicated by the SII, the gap in birth incidence rate of CBD between the highest and the lowest SDI country increased from - 2326.01(95%*CI*: -2670.58 to -1981.43) in1990 to -2296.16(95%*CI*: -2622.67 to -1969.65) in 2021. A significant increase of slope index in NTD was observed from 1990 to 2021, while no significant changed in CBDs and other types. A significant relative inequality in the birth incidence rate of NTD was found and it gets worsened from 1990 to 2021, as the concentration index decreased from - 0.25(95%CI: -0.22 to -0.28) in 1990 to -0.33(95%*CI*: -0.29 to -0.37) in 2021, whereas the relative inequality in CBDs and other types was not pronounced.

Discussion

This study offered a comprehensive analysis of birth incidence rate of CBDs from 1990 to 2021.The findings indicated a decline in both the birth incidence rate and cases of CBDs in 2021 compared to 1990, with an overall downward trend throughout 1990–2021. However, the global birth incidence rate of all types of CBDs, except for OC, was projected to increase from 2022 to 2031 probably. This study examined the relationship between the birth incidence rate of CBDs, its types, and SDI, highlighting existing health inequalities. The analysis revealed a negative correlation between the birth incidence rate of CBDs and SDI, except for DCA and OC. Notably, CHA and NTD exhibited the strongest negative correlations with SDI. Furthermore, NTD demonstrated both absolute and relative inequality across 204 countries.

These findings had significant implications for the public and policymakers. Firstly, the global decline in birth incidence rate from 1990 to 2021 reflected improvements in newborn health, reducing infant mortality and disease burden among children, and contributing to overall population health. The decrease in CBDs enhanced public confidence in health initiatives and policies, encouraging further implementation [18]. However, the study predicted a probable future rise in the birth incidence rate of many types of CBDs. This served as a critical public health warning, highlighting the need for timely action and strengthened control of risk factors to prevent the increase [19]. The projected rise underscored the importance of enhancing international cooperation, with countries sharing data and experienced to tackle the challenge collectively. The correlation and health inequality analysis further stressed the importance of international collaboration. Regions with high birth incidence rate can learn from the successful strategies of regions with low birth incidence rate to refine their own approaches, the focus is on broader strategic measures such as folic acid fortification and rubella vaccination, which are effective and universally affordable interventions [4]. For example, the UK introduced mandatory folic acid fortification in 2022 and would result in an approximately 15–22% reduction in the prevalence of NTD in the forecast [20]. However, given the heterogeneity of health systems and resources, as well as socio-economic and cultural contexts, such single-direction learning may not be effective in the short term, and therefore, strengthening international cooperation, especially in helping disadvantaged countries is worth advocating. Training doctors, nurses and allied health professionals in medical genetics through international cooperation, helping establish the pre-pregnancy prenatal screening mechanisms and medical services during perinatal pregnancy are important measures to promote equality [13]. Addressing health inequality can drive the development of new prevention and treatment methods and diagnostic tools tailored to regional needs, thereby advancing global medical technology [21].

This study was the first to analyze the birth incidence rate of CBDs and its types from 1990 to 2021. The European Surveillance of Congenital Anomalies reported an birth incidence rate of congenital malformations in European countries of approximately 2.39%, [22] Xinyu Li and colleagues assessed the global prevalence of CBDs in children under 14 years of age to be 1,301.66 /100k,[2] Asra Toobaie and colleagues conducted a systematic review estimating the prevalence of congenital anomalies in children in low-income and middle-income countries to be 1,850 /100k [23]. The estimations above were significantly lower than our study's estimation of 5563.72 /100k, the observed difference may stems from our study's inclusion of data from 204 countries, additionally, post-birth deaths due to CBDs were not included in the multi-age prevalence calculations. The results indicated that low SDI region recorded the lowest birth incidence cases and rate, however, low SDI region may face a shortage of medical resources, inadequate infrastructure, poor access to medical services and inadequate birth defect surveillance systems, resulting in inadequate identification and reporting of the disease, which affects the accuracy of the data and may underestimate the reality [11, 12].

From 1990 to 2021, a global downward trend in CBDs was observed across all five SDI regions, with the most significant decline noted in NTD. The decline was likely due to extensive epidemiological evidence indicating the sensitivity of NTD to folic acid. Folic acid supplementation before and during fetal organogenesis has been shown to reduce the risk of NTD development significantly [24]. The widespread implementation of folic acid fortification and supplementation programs in the 1980s contributed substantially to this reduction [25]. Since 2016, however, there was a notable increase in the birth incidence rate of UCA in all five SDI regions. The rise was consistent with previous findings and may be attributed to advancements in ultrasound technology and the introduction of third-trimester fetal ultrasound scanning, which enables earlier detection, however, it can also leads to pregnancy termination, thereby reducing incidence rate [26]. The use of high-frequency probes has also reduced the incidence of false-negative diagnoses [27]. The birth incidence rate of DCA initially decreased but then showed fluctuating increases, necessitating further investigation into the underlying causes. Predictive models indicated a probable continued decline in birth incidence rate of CBDs globally and across all SDI regions, with the most obvious reductions in low SDI region. The trend was likely due to the establishment of newborn screening programs in high-income countries, while low-income countries only recently developed such programs [28]. In low-income areas, the implementation of accessible, cost-effective, and low-tech screening methods can yield significant benefits [29]. Enhancing prenatal testing can rapidly reduce morbidity and improve clinical decision-making processes [30]. Contrary to the global and regional downward trend in CBDs, birth incidence rate of DCA was projected to rise across all five SDI regions probably, requiring increased societal attention. The development of the neonatal digestive tract was a complex process from early embryonic life to birth, necessitating a variety of imaging modalities for evaluation

[31]. A Study suggested that radiological assessments, although crucial for DCA evaluation, must be carefully managed to avoid high morbidity and mortality associated with late diagnosis while minimizing unnecessary radiation exposure [32]. Current research on DCA primarily focuses on diagnosis and treatment, with limited studies on population risk factors and etiology. There is a need for countries to share data to develop more effective prevention and control measures and strategies. Some countries have established national birth defects registration systems that systematically collect and monitor data. Based on this, it is possible to unite multiple countries to build a collaborative network and establish a global congenital malformation research network to promote data sharing and experience exchange, enable researchers and policymakers to more easily access and analyze data to facilitate further research on congenital malformation factors and causes, for example, the Latin American Collaborative Study of Congenital Malformations [33].

Correlation analysis revealed that, in addition to DCA and OC, the birth incidence rate of CBDs and other types were significantly negatively correlated with SDI, aligning with previous studies [14, 27]. Among these CBDs, CHA and NTD demonstrated the strongest association with SDI. This may be attributed to income-related modifiable factors, such as maternal nutritional status or folic acid supplementation programs [34]. Numerous studies showed that folic acid supplementation can prevent NTD and significantly reduce the risk of CHA [35, 36]. Nevertheless, the relationship between the birth incidence rate of CBDs and SDI is uncertain, but it still suggested health inequalities in the birth incidence rate of CBDs across countries with different income levels may exist. Further analysis corroborated that the birth incidence rate of CBDs, excluding DCA and OC, was disproportionately high in economically disadvantaged countries. This aligned with earlier research showing that socio-political-economic factors and policies significantly impacted health and its determinants [37]. A study by Nick Golding et al. highlighted that although development assistance for neonatal and maternal health increased in Africa recently [38], funding remains inadequate, and intervention coverage was lowest in many slower-developing countries [39], potentially exacerbating health inequalities. Given the disparities in health and other factors across countries, local effective studies and the introduction and expansion of cost-effective interventions were essential for addressing health inequalities [40]. However, the lack of clear modifiable causes for certain birth defects, such as DCA and OC, posed challenges for implementing targeted prevention measures globally [41–43]. Significant differences in health inequalities were particularly noted in NTD, likely due to the unequal distribution of health resources across income levels for other types of CBDs. Low-income groups faced persistent barriers, such as limited awareness of CBDs and high fertility rate, maintaining a high absolute burden of NTD [44]. The lack of pre-pregnancy or perinatal health networks in primary healthcare in most developing countries hindered effective early prevention. Conversely, effective and widespread folic acid supplementation education campaigns can help expectant mothers increase their use of folic acid during the perinatal period [45]. However, the coverage of folic acid interventions was significantly better in developed countries compared to developing regions. A review indicated that folic acid supplement intake among women of childbearing age reached 50% in developed countries, while in regions like the Middle East and Africa, the proportion was only 0–34%. As of 2020, only 58 countries worldwide mandated folic acid fortification in staple foods [24, 34]. Therefore, to effectively address disparities in the birth incidence rate of CBDs across different socioeconomic contexts, it is essential to implement comprehensive, evidence-based public health strategies. Policymakers and healthcare professionals should prioritize the development and expansion of maternal and newborn health programs, particularly in low-income regions. This include enhancing access to and awareness of folic acid supplements and other nutritional interventions to reduce the risk of congenital abnormalities such as NTD and CHA. Additionally, investing in robust pre-pregnancy and perinatal care networks can facilitate early detection and prevention of CBDs. International cooperation and increased funding are crucial to support these initiatives and ensure the equitable distribution of health resources and intervention coverage. By adopting a multifaceted approach that addresses both socio-economic and health-related factors, health inequalities can be significantly reduced, leading to improved outcomes and a decrease in the prevalence of CBDs globally.

This study's strength lied in its pioneering analysis of birth incidence rate of CBDs from 1990 to 2021, providing insight into current disease trends. Additionally, analysis of health inequality was employed to identify regional and type-specific disparities in CBDs based on association analysis. However, there were several limitations. The study relied on the GBD database, which recalculated original data to produce new estimates. For example, data for some low SDI countries may based on unverified estimates, which may introduce bias. Additionally, future predictions were solely based on existing data, without accounting for other influencing factors, potentially leading to significant deviations from actual outcomes. Finally, the study did not explore the causes of health inequality, highlighting the need for further investigation to address underlying issues and aid in preventing related diseases.

Base on this, promoting interdisciplinary collaboration among epidemiologists, geneticists, public health experts, and policymakers will integrate diverse perspectives and methodologies, thereby enhancing research robustness. Future research addressing these areas will contribute to a deeper understanding of CBDs and lead to improved prevention and intervention strategies.

Abbreviations

CBDs	Congenital birth defects
ARIMA	Autoregressive Integrated Moving Average
SDI	Socio-Demographic Index
CHA	Congenital heart anomalies
DCA	Digestive congenital anomalies
NTD	Neural tube defects
OC	Orofacial clefts
GBD	Global Burden of Disease
CMLA	Congenital musculoskeletal and limb anomalies
UCA	Urogenital congenital anomalies
TCCBD	Total chromosomal congenital birth defects
APC	Annual percentage change
APPC	Average annual percentage change
RMSE	Root mean square error
MAE	Mean absolute error
MAPE	Mean absolute percentage error

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Supplementary Material 6

Supplementary Material 7

Author contributions

Hanjun Liu and Kebin Chen were responsible for the conceptualization, formal analysis, methodology, and drafting the original manuscript. Tingting Wang contributed to conceptualization, supervision, and manuscript editing. Xiaorui Ruan and Jianhui Wei developed the software for the study and data curation, while Jiapeng Tang and Liuxuan Li handled validation and visualization. Jiabi Qin secured funding, provided supervision, projection administration, and reviewed the manuscript. All authors approved the final manuscript and agreed on its submission for publication.

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Data availability

To download the data used in these analyses, please visit Global Burden of Disease Study 2021 (GBD 2021) Results at https://vizhub.healthdata.org/gbd-results/.

Declarations

Ethics approval and consent to participate

Because the study was based on publicly available dataset, this study was exempted by the ethics committee of the Xiangya School of Public Health of Central South University.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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