

Preplanned Studies

Trends in the Prevalence of Births with Chromosomal Abnormalities — Haidian District, Beijing Municipality, China, 2013–2022

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Summary

What is already known about this topic?

The primary causes of early miscarriage and stillbirth are chromosomal abnormalities (CAs) whose prevalence has been observed to increase in recent years.

What is added by this report?

According to data received from a hospital-based birth-defect surveillance system in the Haidian District, Beijing, there was a significant increase in the prevalence of CAs along with most subtypes from 2013 to 2022. This noted increase in the reported prevalence is potentially attributable to factors such as a rise in maternal age, alongside the enhanced detection efficacy resulting from the utilization of noninvasive prenatal testing.

What are the implications for public health practice?

The escalating prevalence of sex CAs and other previously rare CAs pose novel challenges for genetic counseling and healthcare practitioners. These professionals are tasked with the accurate evaluation and interpretation of detection data, which must then be conveyed appropriately to patients. Furthermore, it is imperative to intensify health education efforts to assist women in making informed treatment decisions, considering the diverse prognoses associated with different CAs.

Chromosomal abnormalities (CAs), which encompass both numerical and structural variants, present as common birth defects. These defects are a predominant factor behind early miscarriage and stillbirth (1). Moreover, they can lead to congenital anomalies such as mental retardation, developmental delays, and multiple malformations in newborns (2). Although recent studies in certain regions have indicated an uptick in the prevalence of CAs, there is

an ongoing need for more research into some underlying subtypes (3–4). In this study, we assessed the trends and prevalence of CAs in Beijing's Haidian District from 2013 to 2022. Our findings revealed a substantial increase in the prevalence of CAs in the Haidian District, with the rate rising from 29.46/10,000 in 2013 to 82.74/10,000 in 2022. Additionally, the prevalence of some subtypes, such as autosomal trisomies, sex CAs (SCAs), and microdeletion/microduplication, evidenced a significant rising trend. The escalating prevalence of SCAs and other previously rare CAs necessitates new strategies for genetic counseling and poses fresh challenges for health professionals. It's critical that healthcare practitioners accurately evaluate these detection results and interpret them appropriately to patients. Strengthening health education initiatives will support women in making informed treatment decisions based on the diverse prognoses of CAs.

This study analyzed data from a hospital-based birth defect surveillance system in the Haidian District, details of which were discussed in a previous publication (5). Briefly, all pertinent healthcare institutions (inclusive of 18 community health service centers, midwifery agencies, and children's hospitals) within the Haidian District are mandated to complete unified forms, registration cards, and report the total count of perinatal infants, alongside detailed individual information on cases of birth defects and infant mortality. Pregnant women were advised to undergo non-invasive prenatal screenings to detect CAs. Owing to technological progression, detection methods have evolved from maternal prenatal serum screening to non-invasive prenatal testing (NIPT). According to the guidelines set out by the Beijing Municipal Health Commission, a prenatal diagnostic rate exceeding 90% is required, with further diagnoses for newborns presenting post-birth abnormalities. The categorization of CAs was conducted in line with the International

Statistical Classification of Diseases and Related Health Problems, 10th Edition. Depending on the clinical examination, different CAs were classified under three primary groups: autosomal trisomies, SCAs, and other CAs (6). CAs of a structural nature (microdeletions, microduplications, translocations, inversions) were further delineated. The annual CAs incidence was calculated by dividing the total count of reported CAs cases by the total number of perinatal infants within that year. A Joinpoint regression model was developed using Joinpoint software (version 4.9.1, Information Management Services, Inc. Calverton, MD, USA) to estimate the average annual percentage change (AAPC) in the prevalence of CAs. Two periods were distinguished according to the Joinpoint regression analysis, and the chi-square test and Fisher's exact test were carried out using R software (version 4.0.5, R Development Core Team, Vienna, Austria) to compare the characteristics distributions in births with CAs between different periods. *P* values equal to or less than 0.05 (two-tailed) were deemed statistically significant.

Between 2013 and 2022, a total of 364,758 births were recorded, along with 1,676 cases of CAs resulting in a prevalence of 45.95 per 10,000 births. The types of CAs and their prevalence over this time period are displayed in Table 1. Over this period, the prevalence

of CAs manifested an increasing trend, escalating from 29.46 per 10,000 in 2013 to 82.74 per 10,000 in 2022, which equates to an AAPC of 13.4% [95% confidence interval (CI): 8.3%, 18.8%].

The prevalence of autosomal trisomies climbed from 19.18 per 10,000 in 2013 to 29.67 per 10,000 in 2022 (AAPC=7.5%, 95% CI: 5.7%, 9.4%). Specifically, trisomy 21 and trisomy 18 syndromes displayed a significant upward trend in prevalence (Trisomy 21: AAPC=6.9%, 95% CI: 4.6%, 9.2%; Trisomy 18: AAPC=8.2%, 95% CI: 4.7%, 11.9%), whereas trisomy 13 syndrome did not (AAPC=1.0%, 95% CI: -17.2%, 23.2%).

SCAs prevalence increased from 4.91 per 10,000 in 2013 to 20.89 per 10,000 in 2022 (AAPC=21.3%, 95% CI: 15.9%, 27.0%). Individual SCAs subtypes (chimerism, 47XXY, 47XYY, 47XXX, 45X) all demonstrated significant increasing trends over the same period, all with AAPC values greater than 0% and *P*-values less than 0.05.

The prevalence of other CAs also increased over the past 10 years (AAPC=22.6%, 95% CI: 16.5%, 30.1%) with significant upward trends observed in microdeletion/microduplication, translocation, and inversion (each with AAPC values greater than 0% and *P*-values less than 0.05).

TABLE 1. Prevalence and trends of chromosomal abnormalities in Haidian District, Beijing, China, from 2013 to 2022 (*N* expressed as 1/10,000).

Chromosomal Abnormalities	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Trend test	
											AAPC (95% CI)	<i>P</i>
Autosomal trisomies	19.18	16.96	20.22	19.71	25.08	23.94	30.34	31.19	29.44	29.67	7.5 (5.7, 9.4)	<0.001
Trisomy 21 syndrome	15.20	13.24	14.62	14.67	18.01	15.77	22.61	23.49	20.57	23.40	6.9 (4.6, 9.2)	<0.001
Trisomy 18 syndrome	3.51	3.31	4.63	4.35	5.93	7.04	4.87	6.16	7.66	5.85	8.2 (4.7, 11.9)	0.001
Trisomy 13 syndrome	0.47	0.41	0.97	0.69	1.14	1.13	2.86	1.54	1.21	0.42	1.0 (-17.2, 23.2)	0.924
Sex chromosome aneuploidies	4.91	5.59	5.36	6.19	10.26	15.49	10.30	15.02	27.03	20.89	21.3 (15.9, 27.0)	<0.001
Sex chromosome chimerism	0.70	1.86	0.97	1.83	2.51	2.25	1.43	1.93	4.44	2.93	13.4 (5.5, 22.0)	0.004
47XXY	1.64	1.66	1.22	1.37	3.19	3.94	4.29	5.78	10.49	6.27	26.4 (18.0, 35.4)	<0.001
47XYY	0.47	0.41	0.49	0.92	0.91	1.97	0.86	1.54	3.63	2.51	25.8 (18.3, 33.7)	<0.001
47XXX	0.47	0.62	0.49	0.46	1.14	3.38	2.58	1.54	2.82	1.67	22.6 (7.2, 40.1)	0.008
45X	1.64	1.03	1.71	1.15	1.37	2.82	1.14	2.31	1.61	2.93	6.6 (2.8, 10.5)	0.004
Other chromosomal abnormalities	5.38	6.20	5.85	7.34	11.18	11.82	18.03	22.74	25.40	35.10	22.6 (15.6, 30.1)	<0.001
Microdeletion/microduplication	1.64	1.45	3.9	3.21	5.02	3.94	9.73	13.1	16.94	19.22	34.9 (29.3, 40.6)	<0.001
Translocation	1.87	2.48	0.49	1.15	3.19	3.38	3.72	4.62	4.03	7.52	20.8 (5.7, 38.0)	0.012
Inversion	0.70	1.03	0.73	0.46	2.05	1.97	2.29	1.93	2.42	5.85	23.2 (11.6, 36.0)	0.001
Others	1.17	1.24	0.73	2.52	0.92	2.53	2.29	3.09	2.01	2.51	12.5 (7.0, 18.3)	0.001
Total	29.46	28.76	30.95	32.77	44.91	49.85	58.39	66.63	77.45	82.74	13.4 (8.3, 18.8)	<0.001

Abbreviation: AAPC=average annual percent change; CI=confidence interval.

TABLE 2. Trends in the annual prevalence of chromosomal abnormalities in Haidian District, Beijing, China, from 2013 to 2022 using Joinpoint regression analysis.

Segments*	Year	APC (95% CI)	P
Trend 1	2013–2015	3.4 (–20.2, 33.9)	0.754
Trend 2	2015–2022	16.4 (13.5, 19.5)	<0.001
Full range	2013–2022	13.4 (8.3, 18.8)	<0.001

Abbreviation: APC=annual percentage change; CI=confidence interval.

* The implementation of universal two-child policy was in 2016 and the application of noninvasive prenatal testing was 2017.

Table 2 illustrates an inflection point in CAs prevalence identified by Joinpoint regression modeling in 2015. The initial trend indicates an escalation in annual prevalence from 29.46/10,000 in 2013 to 30.95/10,000 in 2015 (APC=3.4%, 95% CI: –20.2%, 33.9%). The subsequent trend demonstrates a significant upsurge from 30.95/10,000 in 2015, escalating to 77.45/10,000 in 2022 (APC=16.4%, 95% CI: 13.5%, 19.5%).

Table 3 delineates the variation in characteristics of CAs across distinct periods. Among all CAs instances, significant increases from 2013–2015 to 2016–2022 were observed for maternal age ($P<0.001$), gravidity ($P=0.002$), parity ($P<0.001$), and prenatal diagnostics ($P<0.001$). For trisomy 21 syndrome cases specifically, disparate distributions in maternal age, parity, gestational weeks, prognosis, therapeutic abortion, and timing of diagnosis were evident across varying periods (all $P<0.05$). In SCAs scenarios, a marked increase in prenatal diagnostics was shown, from 87.7% in 2013–2015 to 98.9% in 2016–2022 ($P<0.001$). Furthermore, in cases involving microdeletion and microduplication, there was an observed augmentation in gravidity ($P=0.020$) and the rate of therapeutic abortion ($P=0.026$) during the period from 2013–2015 to 2016–2022.

DISCUSSION

Data derived from a hospital-based birth-defect surveillance system in Haidian District, Beijing indicates a steady rise in the prevalence of CAs over the past decade. The data further reveals a significant increase in the prevalence of most CAs subtypes from 2013 to 2022. Interestingly, the year 2015 marked a major turning point in this trend wherein the prevalence growth rate significantly escalated post-2015.

Globally, CAs occur in approximately 4 to 9 out of every thousand newborns (6). In the Haidian District of Beijing, the prevalence of CAs is relatively low, with 4.595 per thousand. It is important to mention,

however, that this prevalence has seen a steady increase, reaching 8.274 per thousand in 2022. Due to regional differences in detection rates and capabilities, it would be inaccurate to directly compare the prevalence of CAs between different regions. Nonetheless, a similar increasing trend in prevalence, as seen in this study, has been reported in several prior studies. For instance, the prevalence of trisomy 21, trisomy 18, and trisomy 13 syndromes in Europe showed an escalation between 2005 and 2021 (3). In Zhejiang Province, the overall prevalence of CAs rose from 1.209 per thousand to 3.922 per thousand between 2014 and 2020, with varying degrees of increase in the prevalence of trisomy 21 syndrome, SCAs, and microdeletions/microduplications (4). Similarly, in Guangdong Province, the prevalence of trisomy 21 syndrome surged from 0.465 per thousand to 1.364 per thousand between 2011 and 2018 (7).

In our investigation, it was observed that the maternal age for children suffering from CAs during the period 2016–2022 was statistically higher compared to 2013–2015. This change coincided with China's transition from a one-child to a universal two-child policy in 2016. As a result, there was a noticeable increase in the percentage of pregnancies associated with older mothers, multiple pregnancies, and multiparous women from 2016 to 2022 in contrast to the numbers recorded between 2013 and 2015. Earlier research determined that advanced maternal age significantly raises the risk for CAs (8). Consequently, it can be posited that the shift in birth policy may have indirectly increased maternal age, gravidity, and parity, thereby causing a surge in the prevalence of CAs post-2016 (9).

Conversely, the observed surge in reported cases of CAs might represent advancements in prenatal diagnostic methods in Haidian District and increased awareness among expectant mothers. The National Health Commission of the People's Republic of China initiated a nationwide pilot program for this technology in 2016 and the NIPT technology was applied in 2017 in Beijing (10). Evidently, NIPT

TABLE 3. Variations in characteristics of chromosomal abnormality cases over select time periods in Haidian District, Beijing, China, *n* (%).

Variable	Total CAs		P*	Trisomy 21 syndrome		P*	SCAs		P*	Microdeletions/microduplication			P*
	2013–2015	2016–2022		2013–2015	2016–2022		2013–2015	2016–2022		2013–2015	2016–2022	ns	
Total	392	1,284		189	444		70	280		30	208		
Age, years			<0.001			0.006			0.077				0.054
≤30	113 (31.0)	265 (20.7)		45 (26.0)	67 (15.2)		26 (37.1)	69 (24.6)		15 (50.0)	60 (28.8)		
30–35	124 (34.0)	456 (35.7)		54 (31.2)	148 (33.5)		27 (38.6)	114 (40.7)		10 (33.3)	84 (40.4)		
>35	128 (35.1)	557 (43.6)		74 (42.8)	227 (51.4)		17 (24.3)	97 (34.6)		5 (16.7)	64 (30.8)		
Gravidity			0.002			0.065			0.211				0.020
1	154 (39.3)	399 (31.1)		73 (38.6)	138 (31.1)		33 (47.1)	109 (38.9)		16 (53.3)	66 (31.7)		
≥2	238 (60.7)	885 (68.9)		116 (61.4)	306 (68.9)		37 (52.9)	171 (61.1)		14 (46.7)	142 (68.3)		
Parity			<0.001			<0.001			0.100				0.745
Nulliparous	193 (49.2)	433 (34.5)		103 (54.5)	173 (39.0)		33 (47.1)	102 (36.4)		11 (36.7)	70 (33.7)		
Multiparous	199 (50.8)	851 (66.3)		86 (45.5)	271 (61.0)		37 (52.9)	178 (63.6)		19 (63.3)	138 (66.3)		
Gestational week			0.675			<0.001			0.888				0.134
<28	284 (72.4)	944 (73.5)		155 (82.0)	425 (95.7)		47 (67.1)	184 (65.7)		14 (46.7)	127 (61.1)		
≥28	108 (27.6)	340 (26.5)		34 (18.0)	19 (4.3)		23 (32.9)	96 (34.3)		16 (53.3)	81 (38.9)		
Number of embryos			0.291			0.997			0.778				0.656
Single birth	342 (94.0)	1,222 (95.3)		165 (95.9)	425 (95.9)		62 (95.4)	260 (93.2)		28 (96.6)	200 (96.6)		
Multiple births	22 (6.0)	60 (4.7)		7 (4.1)	18 (4.1)		3 (4.6)	19 (6.8)		1 (3.4)	7 (3.4)		
Prognosis			0.510 [†]			<0.001 [†]			1.000 [†]				1.000 [†]
Live birth	88 (24.2)	273 (21.4)		26 (15.1)	10 (2.3)		20 (30.8)	88 (31.5)		12 (41.4)	47 (22.7)		
Early fetus loss and stillbirths	274 (75.3)	998 (78.1)		146 (84.3)	432 (97.5)		45 (69.2)	190 (68.1)		16 (55.2)	155 (74.9)		
Early neonatal deaths	2 (0.5)	7 (0.5)		1 (0.6)	1 (0.2)		0 (0.0)	1 (0.4)		1 (3.4)	5 (2.4)		
Therapeutic abortion			0.270			<0.001			0.774				0.026
No	93 (25.5)	292 (22.8)		27 (15.7)	14 (3.2)		20 (30.8)	91 (32.6)		13 (44.8)	52 (25.1)		
Yes	271 (74.5)	990 (77.2)		145 (84.3)	429 (96.8)		45 (69.2)	188 (67.4)		16 (55.2)	155 (74.9)		
Time of diagnosis			<0.001			<0.001			<0.001				0.741
Prenatal	324 (89.0)	1,249 (97.4)		146 (84.9)	438 (98.9)		57 (87.7)	276 (98.9)		28 (96.6)	197 (95.2)		
Postpartum	40 (11.0)	33 (2.6)		26 (15.1)	5 (1.1)		8 (12.3)	3 (1.1)		1 (3.4)	10 (4.8)		

Abbreviation: CAs=chromosomal abnormalities; SCAs=sex chromosomal abnormalities.

* Differences between the 2013–2015 period and 2016–2022 period, using Chi-square test.

† Differences between the 2013–2015 period and 2016–2022 period, as determined by Fisher's exact test.

technology exhibits high performance in early detection of CAs, managing to identify certain variants of CAs that proved challenging via traditional methods. Owing to its elevated sensitivity, the prevalence of missed diagnosis prior to pregnancy is minimized, which may partially account for the rising prevalence of CAs noted in this study.

The NIPT not only enhances the efficacy of detection for autosomal trisomies, but also proves useful in identifying certain types of SCAs, such as 47 XYY and 47 XXY, and other CAs (4). Ethical considerations necessitate that any decision to proceed with therapeutic abortion for CAs must fully respect the patient's wishes. Therefore, healthcare practitioners need to deliver individualized and detailed genetic counseling based on the detection information. For severe cases like trisomy 21 syndrome, healthcare practitioners may provide conclusive advice allowing the patient to consider therapeutic abortion before the 28 weeks gestation mark. However, certain CAs such as some SCAs subtypes and structural CAs are neither fatal nor severely debilitating. Here, practitioners' advice should take into account a variety of factors such as prognosis, the patient's physical condition, and financial capabilities. The final decision rests with the patient whether to proceed with abortion or explore different interventions. Limited counselling or insufficient explanation can lead to unnecessary abortions resulting in unwarranted intervention. The exemplary detection capacity of NIPT has led to an uptick in the proportion of hitherto rare SCAs and other CAs, posing fresh challenges for genetic counselling and healthcare practitioners.

Our findings indicate that the SCA abortion rate did not considerably rise post-2016, an encouraging sign. However, it is crucial to note that the abortion rate for microdeletion/microduplication was higher between 2016–2022 compared to 2013–2015. Looking ahead, the focus must be on increasing awareness and education among expectant women for a proper understanding. Healthcare practitioners must also strive for accurate interpretation and evaluation of test information, to aid patients in making appropriate treatment decisions in light of the varying prognoses associated with CAs.

The present study possesses several notable strengths. Primarily, Haidian District boasts a 100% rate of hospital-based delivery, making the district's hospital surveillance data an accurate representation of the population. Secondary strength lies in the district's

high level of medical care, coupled with the established diagnostic proficiency of affiliated midwifery organizations. The deployed surveillance system, with its extensive review and rejection mechanisms for diagnostic results, bolsters data reliability at both the district and municipal levels. Moreover, the classification of CAs within the surveillance system — trisomy 21, trisomy 18, trisomy 13 syndrome, SCAs, and other CAs — was subdivided into more precise subtypes. This allows for a more nuanced analysis of CAs prevalence and also aids in enhancing future classification systems.

This study encompasses several limitations. Primarily, as a regional observational research, the findings are specifically indicative of the urban region in Beijing and may not be comprehensively representative of either the complete Beijing populace, or China overall. Additionally, the study did not incorporate an exhaustive categorization of structural CAs. Lastly, certain data categories such as specific exposure factors were omitted from collection in this research, limiting the study's scope to merely detailing the distribution of CAs rather than identifying potential risk factors.

The prevalence of CAs in Haidian, Beijing, has markedly risen from 2013 to 2022. This increase may be ostensibly linked to a rise in advanced maternal age and the utilization of NIPT. Heightened detection rates of CAs can expedite treatment for pregnant women diagnosed with poor prognosis conditions such as trisomy 21 syndrome, thus alleviating their burden. Conversely, attention must also be accorded to other CAs, such as SCAs, and women should be educated to form an accurate comprehension of these conditions. Achieving this requires healthcare practitioners to possess a comprehensive understanding of the advantages and disadvantages of prenatal diagnostic methods, patient preferences, and ethical evaluations.

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