

Original Article

Human sex ratio at amniocentesis and at birth in Taiwan

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Abstract

Objectives: An increase in the proportion of male-to-female live births has raised concerns in Taiwan. Disclosure of fetal sex during prenatal screening is not allowed by the Taiwan government. Fetal sex annotation in clinical genetic reports is also prohibited. This study tested the hypothesis that the male-to-female sex ratio at amniocentesis should be lower than the sex ratio at birth, if a certain percentage of female fetuses are being selectively aborted after amniocentesis. Therefore, we examined the differences between fetal sex ratio at amniocentesis at a tertiary medical center in southern Taiwan and the nationwide sex ratio at birth in Taiwan from 1992 to 2011.

Materials and Methods: Data of normal male and female karyotypes during the study period were collected from the cytogenetic laboratory of the National Cheng Kung University Hospital (NCKUH) in southern Taiwan. Data of sex ratio at birth nationwide in Taiwan were obtained from the Department of Statistics, Ministry of the Interior, Taiwan. We calculated 95% binominal confidence intervals for the sex ratios and differences between fetal sex ratio at amniocentesis, and nationwide sex ratio at birth were tested by the χ^2 test and Bonferroni correction.

Results: The nationwide sex ratio at birth ranged from 1.07 to 1.11 during the period from 1992 to 2011 in Taiwan, with the highest in 2004 and the lowest in 1993. The fetal sex ratio at amniocentesis at NCKUH ranged more widely (0.82–1.28), with the lowest in 1993 and the highest in 2007. After regression analysis, both trends of sex ratio at amniocentesis during midtrimester and at birth were not significantly increased by years. Furthermore, the sex distribution at amniocentesis during midtrimester did not differ significantly from the nationwide sex ratio at birth (1.113 vs. 1.092, $p = 0.151$).

Conclusions: The results showed that sex ratio was already skewed toward male at midtrimester. Our data imply that artificial sex selection, if it were present, might have already emerged prior to the timing of amniocentesis. However, more large nationwide studies on sex ratios in Taiwan are warranted.

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Keywords: prenatal sex determination; sex discrimination; sex ratio

Introduction

Sex ratio, defined as the ratio of males to females in a population, is assumed to be close to 1:1. In humans, the

natural sex ratio at birth remains a controversial issue for biologists. Considering the fact that male fetuses are more vulnerable to life-threatening insults than females, it has been postulated that the natural sex ratio at birth should be slightly higher than 1. In reality, the worldwide sex ratio at birth is approximately 105 boys per 100 girls [1–3]. However, statistics from a number of government databases have shown that sex ratios at birth have been skewed recently [4–7]. Human sex ratio after birth has also been reported to be relevant to the variation of life expectancy and mortality [8].

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Generally, sex ratios at birth are lower than 1 in developed countries at higher altitudes, such as the United States, Canada, and Europe [4–7]. By contrast, sex ratios at birth are consistently higher than 1 in developing countries with cultural preferences that favor the birth of males over females. In Asian countries, such as China, the predominant male-to-female ratio at birth has been postulated as a result of selective abortion of female fetuses by prenatal sex determination [9,10]. Skewed sex ratios have also been reported in immigrants from India to Norway [11]. However, the sample sizes in that study were too small to draw definitive conclusions of a preference for sex-selective abortion among mothers of Indian origin [11].

Notably, in China, a country in which the birth of more than one baby is prohibited by strict national policy, Zhu et al have found that the ratio of boys to girls in rural areas of China was as high as 120:100 [10]. Sex ratios in several countries have also shown significant transitions in the past few decades [6], and skewing of sex ratios at birth has been reported to be an indicator of sex discrimination, which may violate basic human rights [9].

An increase in the proportion of male-to-female live births has raised concerns in Taiwan recently. Prenatal fetal sex disclosure is strictly prohibited in all clinical settings by the Taiwan government. Clinicians have been officially banned from responding directly to parents who ask the question “Is it a girl or a boy?” In addition, fetal sex annotation has also been prohibited in all clinical genetic reports after August, 2011 [12].

In order to investigate the fetal sex ratio issue, the objective of this study was to assess the difference between fetal sex ratio at a tertiary medical center and the nationwide sex ratio at birth in Taiwan. The null hypothesis of this study is that fetal sex ratio at amniocentesis is not different to the sex ratio at birth. On the contrary, the alternative hypothesis is that fetal sex ratio at amniocentesis is different from the sex ratio at birth, which implies a certain percentage of female fetuses are being selectively aborted after fetal sex has been disclosed at midtrimester.

Material and methods

Fetal sex ratio at amniocentesis

All prenatal karyotyping results obtained during the period from 1992 to 2011 at the Cytogenetic Laboratory of the National Cheng Kung University Hospital (NCKUH), a tertiary medical center in southern Taiwan, were retrieved and analyzed. Fetal sex ratios at amniocentesis were calculated by dividing the number of fetuses with a normal male karyotype (46,XY) by the number of fetuses with a normal female karyotype (46,XX). Fetuses with aneuploidy or translocations were excluded. Maternal and fetal characteristics that were analyzed in this study included maternal age, indications for amniocentesis, date of amniocentesis, and gestational age of the fetus at the time of amniocentesis. This study was approved by the institutional review boards from NCKUH.

Sex ratio at birth

The sex ratio at birth in each year of the study period was defined as the ratio of all boys to all girls aged <1 year registered in the Department of Statistics, Ministry of the Interior, Administrative Yuen, Taiwan, ROC.

Statistical analysis

We calculated the 95% binominal confidence intervals (CIs) for the sex ratios by using the 95% CI for the proportion of male births or fetuses with normal male karyotype (pf) with a variance of pf (1 – pf). The sex ratios and 95% binominal CIs were determined with the quadratic formula as reported by Spiegel (1961) for binomial CIs for proportions. Differences between fetal sex ratio at amniocentesis and sex ratio at birth were tested by the χ^2 test and Bonferroni corrections [13]. Differences were considered statistically significant with a *p* value <0.05.

Results

As illustrated in Fig. 1, the trends in sex ratio in Taiwan during the period from 1992 to 2011 were examined by regression analysis. First, the nationwide sex ratio at birth was not increased or decreased for 20 years ($y = 0.0002x + 0.6253$; $R^2 = 0.0334$, NS). Second, the sex ratio at amniocentesis at NCKUH during the 20 years was not significantly increased ($y = 0.091x - 17.108$; $R^2 = 0.2394$, NS). Although the fetal sex

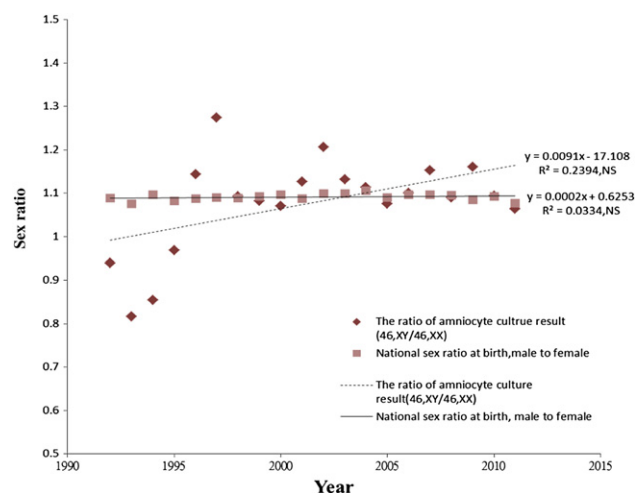


Fig. 1. Trends of sex ratio at amniocentesis and at birth. ■ The national sex ratio at birth was defined as the ratio of all boys to all girls aged <1 year registered in the Department of Statistics, Ministry of the Interior. Data were retrieved from Statistical Year Book of Interior, published by Department of Statistics, Ministry of the Interior, Executive Yuan, Taiwan, R.O.C., at <http://sowf.moi.gov.tw/stat/year/elist.htm>, accessed on January 15, 2012. ◆ Fetal sex ratios at amniocentesis were calculated by dividing the number of fetuses with a normal male karyotype (46, XY) by the number of fetuses with a normal female karyotype (46, XX). All prenatal karyotyping results were obtained during the period 1990 to 2010 at the cytogenetic laboratory of the National Cheng Kung University Hospital but fetuses with aneuploidy or translocations were excluded. NS = not significant.

ratio at amniocentesis seemed to increase more than the human sex ratio at birth nationwide during the study period of two decades, the difference in both trends was not statistically significant.

As shown in Table 1, the nationwide sex ratio at birth in Taiwan remained constant at 1.08 during the period from 1992 to 2011, with the highest at 1.1057 in 2004 and the lowest at 1.0759 in 1993. Overall, there was no significant difference in sex distribution between the NCKUH data and the nationwide data (1.113 vs. 1.092, $p = 0.110$). Although the fetal sex ratios at amniocentesis were significantly different to the nationwide sex ratio at birth in 1994, 1997, and 2002, as tested by the χ^2 test using the threshold of $p \leq 0.05$, all were nonsignificant after Bonferroni correction using the corrected threshold of $p \leq 0.001$.

In addition, the average maternal age at amniocentesis ranged from 32.4 years to 35.33 years at NCKUH from 1992 to 2011, while the average maternal age ranged from 26.4 years in 1998 to 29.8 years in 2008. Of interest, the maternal age at amniocentesis at NCKUH was higher than that nationwide at birth because more than half the mothers received amniocentesis due to advanced maternal age.

Discussion

The trends in sex ratio at birth in Taiwan during the period from 1992 to 2011 remained constant at 1.08. Our result shows that the fetal male-to-female sex ratio at amniocentesis increased no more than the sex ratio of newborn babies in

Taiwan. In addition, the mothers who underwent prenatal diagnosis were older. Our findings imply that the so-called selective abortion of female fetuses after amniocentesis is not true; at least at a tertiary medical center in southern Taiwan, where people are considered to be more traditional and conservative than northern Taiwan.

Changes in sex ratio at birth have been attributed to many different factors, including maternal age at menarche, parental ages, birth order, race, and preference of boys or girls [3,5,7,14–16]. By contrast, data from most countries in Europe and North America show that the male-to-female ratio of second-order births is lower than that of first-order births [4,6]. Globally, the differences in human natal sex ratio are positively correlated with life expectancy, indicating that the natal sex ratio is influenced by existing environmental conditions and perceived future survival [8,17]. Advocates and governments seeking to reverse this imbalance have prohibited sex detection tests and/or sex-selective abortion [9] in the hope that these measures would reverse the trend. Such policies have been difficult to enforce, however, and have met with only limited success [18,19].

Taiwan is located off the coast of southeastern China and shares a Han Chinese heritage. One of the most distinguishing culture features of the Han Chinese, both in China and in Taiwan, is the existence of a patrilineal society in which married daughters belong to the husband's family, and families tend to prefer boys to girls. In some instances, in China as well as in countries with low fertility rates, data on sex ratio at birth are affected by generalized and systematic under-

Table 1
Comparison of sex ratio at amniocentesis and at birth.

Year	Maternal age at amniocentesis (y; mean \pm SD)	Numbers of karyotype reports of fetus			Boys/girls <1 y old in national population in Taiwan ^a			
		46,XY	46,XX	Sex ratio at amniocentesis (95% CI) ^c	Boys born	Girls born	Sex ratio at birth (95% CI) ^b	<i>p</i> value
1992	34.45 \pm 4.25	47	50	0.94 (0.63–1.40)	160,372	147,360	1.09 (1.08–1.10)	0.471
1993	33.65 \pm 4.80	71	87	0.82 (0.60–1.12)	159,265	148,027	1.08 (1.07–1.08)	0.083
1994	32.46 \pm 6.48	117	137	0.85 (0.67–1.09)	153,609	140,085	1.10 (1.09–1.11)	0.047 ^c
1995	32.50 \pm 4.94	150	155	0.97 (0.77–1.21)	157,466	145,612	1.08 (1.07–1.09)	0.332
1996	32.40 \pm 4.93	312	273	1.14 (0.97–1.34)	158,284	145,553	1.09 (1.08–1.10)	0.549
1997	32.65 \pm 5.01	455	357	1.28 (1.11–1.46)	160,299	147,107	1.09 (1.08–1.10)	0.027 ^c
1998	32.40 \pm 5.15	568	520	1.09 (0.97–1.23)	132,759	122,017	1.09 (1.08–1.10)	0.949
1999	32.87 \pm 4.87	848	784	1.08 (0.98–1.19)	141,105	129,112	1.09 (1.09–1.10)	0.835
2000	33.12 \pm 4.88	983	918	1.07 (0.98–1.17)	153,054	139,670	1.10 (1.09–1.10)	0.616
2001	32.40 \pm 5.13	1019	905	1.13 (1.03–1.23)	128,338	118,043	1.09 (1.08–1.10)	0.445
2002	32.43 \pm 5.11	1024	849	1.21 (1.10–1.32)	123,895	112,792	1.10 (1.09–1.11)	0.045 ^c
2003	32.62 \pm 5.10	904	799	1.13 (1.03–1.24)	114,018	103,438	1.10 (1.09–1.11)	0.593
2004	32.61 \pm 5.03	989	888	1.11 (1.02–1.22)	108,663	98,273	1.11 (1.10–1.12)	0.876
2005	32.74 \pm 5.52	936	870	1.08 (0.98–1.18)	101,864	93,467	1.09 (1.08–1.10)	0.785
2006	33.28 \pm 5.11	1025	932	1.10 (1.01–1.20)	100,859	92,028	1.10 (1.09–1.11)	0.939
2007	35.33 \pm 1.15	1278	1,109	1.15 (1.06–1.25)	100,434	91,587	1.10 (1.09–1.11)	0.229
2008	NA	1268	1,164	1.09 (1.01–1.18)	98,038	89,530	1.10 (1.09–1.11)	0.899
2009	33.54 \pm 4.33	1318	1,136	1.16 (1.07–1.26)	94,987	87,612	1.08 (1.07–1.09)	0.096
2010	33.49 \pm 4.61	1301	1,189	1.09 (1.01–1.18)	82,126	75,156	1.09 (1.08–1.10)	0.974
2011	33.68 \pm 4.13	1310	1,232	1.06 (0.98–1.15)	101,943	94,684	1.08 (1.07–1.09)	0.755
Total		15,923	14,354	1.11 (1.08–1.13)	788,014	722,337	1.09 (1.09–1.09)	0.151

CI = confidence interval; NA = not available.

^a Data retrieved from <http://sowf.moi.gov.tw/stat/year/elist.htm>; accessed January 15, 2012.

^b 95% CI for the proportion of male births (pf) with a variance of pf (1 – pf).

^c All were nonsignificant after Bonferroni correction.

reporting of female births and, in some cases, even misreporting of the sex [20,21]. Previous studies suggest a growing imbalance in China's sex ratio at birth, which is most likely due to an increase in sex-selective abortion [20]. Contrary to China with its strict one-child policy, people in Taiwan are encouraged to have two or more children, especially if a girl is born first. In Taiwan, the fertility rate, defined as the number of babies born every year divided by the number of women during childbearing age, has gradually decreased from 7.045 in the 1940s to 1.030 in 2010 [22]. In fact, the decision by parents not to have another child if their first child is a boy may more accurately explain the higher sex ratio than sex-selection abortion as a result of fetal sex detection [18]. A couple, therefore, might choose to have only one baby if they already have a boy, whereas a couple whose first child is a girl might attempt to have a son in the following pregnancy [23].

Our data obtained from individuals with a cultural preference for boys show that sex ratio is already skewed at amniocentesis at midtrimester. The data imply that artificial sex selection, if it were present, might occur prior to amniocentesis.

To the best of our knowledge, no previous reports on the prenatal human sex distribution issue have been published in Taiwan. Our series might be the first one to investigate the sex ratio at amniocentesis and at birth. Our data showed no difference between the sex ratio at amniocentesis and that at birth. However, our study had some limitations. First, the sex ratio at birth might vary with maternal age, and the mothers in the prenatal group at NCKUH were markedly older than the mothers in the general population in Taiwan. Second, the cytogenetic database does not include information on the birth order or the sex of babies previously born in the same families.

In conclusion, we present the trends of sex ratios at the midtrimester and at birth in Taiwan from 1992 to 2011. The results show no difference between the sex ratios at amniocentesis at NCKUH and at birth in Taiwan for two decades. From this series, we conclude that the annotation of fetal sex by prenatal cytogenetic reports has no effect on the sex ratio at birth. Further studies are required to draw a definite conclusion between these links.

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