Is There a Familial Tendency for Same Sex Offspring? A Lesson Learned from a Large Non-Selected Israeli Population

Gilad Karavani MD[1]*, Adi Reuveni Salzman MD[1]*, Eliana Ein-Mor PhD[2], Uri Pinchas Dior MD[1] and Shay Porat MD PhD[1]

[1]Department of Obstetrics and Gynecology and [2]Braun School of Public Health, Hadassah–Hebrew University Medical Center, Jerusalem, Israel

ABSTRACT

Background: While the ratio of male-to-female births (sex-ratio at birth [SRB]) in humans is remarkably stable on the population level, there are many families with multiple same-sex offspring.

Objectives: To identify a putative sub-population with skewed SRB and explore potential factors affecting the SRB.

Methods: A retrospective cohort study including 66,054 families with up to nine same-sex offspring evaluated between 2003 and 2015 at Hadassah-Hebrew University Medical Center. Outcome measures were observed prevalence and SRB of families with up to nine same-sex offspring in a single family. Analyses included the effect of parity, month and year of delivery, inter-delivery interval, and presence of a sequence of previous same-sex offspring on the SRB.

Results: The study comprised 193,411 live-born babies with SRB of 1.057 in favor of males. The proportion of SRB in families with up to nine same-sex offspring did not differ from the calculated presumed proportion. Furthermore, none of the tested factors (parity, month and year of delivery, inter-delivery interval, and the sequence of previous same-sex offspring) were significantly associated with SRB.

Conclusions: SRB was not associated with any of the tested demographic characteristics. We could not identify a skew in SRB even in families with up to nine consecutive same sex offspring. This finding suggests that in the majority of the population the chance of a male or female fetus in each pregnancy remains similar in every pregnancy, regardless of any of the tested variables.

IMAJ 2020; 22: 354–354

KEY WORDS: male-to-female ratio, offspring, sex-ratio at birth (SRB), sibship

In almost all human populations, there is a slight excess of males at birth. On a population level, sex-ratio at birth (SRB) under normal conditions is strikingly stable, seldom varying significantly from values roughly between 1.020 and 1.083 [1,2]. Modern reproductive technology has made prenatal diagnosis widely accessible and has led to recent skewed SRB in certain populations [3].

Biological and environmental factors that have been suggested to alter the SRB and increase the odds of giving birth to a boy include older maternal age [2], high maternal and/or paternal social rank, female assertiveness [4], increased frequency of sexual intercourse [5], and birth during the summer months [1]. Factors that were associated with increased odds of giving birth to a girl included higher birth order, older paternal age [2], geographic origin [6], and certain paternal occupations [7,8].

The SRB of mammals is related to paternal and maternal hormone levels at conception. According to this hypothesis, high concentrations of testosterone and estrogen increase the probability of a giving birth to a boy and high concentrations of gonadotropins and progesterone increase the probability of giving birth to a girl [9,10]. Therefore, it has been hypothesized that the probability of a conceiving a boy is higher early and late in the menstrual cycle and the probability of conceiving a girl is higher in the middle of the cycle. By analyzing families with up to nine consecutive offspring of the same sex we aimed to assess the possible existence of skewing toward a specific sex of offspring in certain families.

PATIENTS AND METHODS

STUDY POPULATION

This retrospective cohort study included all parturients with at least one live-born infant who gave birth at one of two campuses of a tertiary medical center between 2003 and 2015. Data were collected from the comprehensive perinatal database of the tertiary medical center. Data regarding the sex of each offspring of the family as well as the sex of the current baby were obtained

*The first and second authors contributed equally to this study

for each parturient on admission to the delivery room. To avoid duplicity, data were collected only from the most recent delivery of each parturient.

Inclusion criteria included women with live newborn babies, singletons in current and all past deliveries, and complete records. We excluded from the analysis parturients who underwent missed abortions, termination of pregnancy, intrauterine demise, and molar pregnancies.

ANALYSIS OF THE EFFECT OF PARITY ON THE SRB

We calculated the SRB for the entire population including all offspring from all families that were born during or before the study period (reference SRB). We then calculated the SRB for each level of parity and compared it to the reference SRB.

SEARCH FOR A SUBPOPULATION WITH NATURAL PREDILECTION TOWARD A SPECIFIC SEX OF OFFSPRING

We hypothesized that if a subset of the population has a natural predilection toward a specific sex, then their relative representation in the entire population will be higher than expected. Hence, we calculated the prevalence of same-sex offspring families with up to nine consecutive offspring and compared that to the expected prevalence based on the reference SRB. Next, we calculated the SRB of the next-born offspring in same-sex offspring families and compared to the reference SRB.

ANALYSIS OF THE EFFECT OF THE CALENDAR MONTH OF DELIVERY, YEAR OF DELIVERY, AND INTER-DELIVERY INTERVAL ON THE SRB

We calculated the effect of the calendar month of the delivery (as a proxy to the calendar month of conception), the year of delivery, and the inter-delivery interval (as a proxy for maternal age) on the SRB of all babies born during the study period.

STATISTICAL ANALYSIS

Dichotomous variables were analyzed with the chi-square test to determine whether ratios of each outcome differed from expected. As families with unisexual sibship of a certain number of offspring were utilized for multiple comparisons (comparisons of one for each additional offspring) the Bonferroni correction was applied to control for the family-wise error rate. Statistical analyses were performed using the IBM Statistical Package for the Social Sciences statistics software, version 21 (SPSS, IBM Corp, Armonk, NY, USA). A P value of < 0.05 was considered significant.

ETHICS APPROVAL

The study was approved by the Human Research Ethics Committees of the Hadassah University hospital (IRB approval number: HMO-0620-15) and conforms to the provisions of the Declaration of Helsinki.

Table 1. Influence of parity on sex-ratio at birth

	Expected*		Observed				
P value	Females	Males	Total	SRB	Females	Males	Parity
0.429	32116	33950	66066	1.064	32014	34052	0
0.672	24354	25746	50100	1.061	24307	25793	1
0.444	16433	17371	33804	1.048	16503	17301	2
0.396	9461	10001	19462	1.044	9520	9942	3
0.294	5229	5527	10756	1.036	5283	5473	4
0.609	2960	3129	6089	1.071	2940	3149	5
0.355	1675	1771	3446	1.091	1648	1798	6
0.767	946	1001	1947	1.043	953	994	7
0.404	539	570	1109	1.005	553	556	8
0.513	307	325	632	1.114	299	333	9
				1.057	94020	99391	Total

*Expected number of males and females was calculated by using the reference SRB ratio (1.057) controlling for the same total number of infants n=193,411.
SRB = sex-ratio at birth

RESULTS

Of the 193,411 eligible babies born to 66,066 families, 99,391 (51.3%) were male and 94,020 (48.7%) were female, representing an SRB of 1.057 in favor of males. This ratio was referred to as the reference ratio.

To analyze the effect of parity we calculated the SRB per each parity level: 1–10. The SRB of the first to tenth delivery ranged between 1.005–1.114, representing a male and female fraction of 50.14–52.69% and 47.31–49.86%, respectively. None of the calculated SRBs differed significantly from the reference SRB [Table 1] signifying no effect of parity.

We then compared the observed prevalence of same-sex families (out of all families with a similar number of offspring) with the expected prevalence. After a Bonferroni correction none of the comparisons was statistically significant [Table 2].

The SRB of the subsequent offspring in families with a unisexual sibship of only-male or only-female offspring remained similar to the reference SRB, regardless of the number of previous same-sex offspring [Table 3].

A separate analysis, including variables that were previously reported to affect SRB was conducted. This analysis also did not show any significant differences between the expected and observed SRBs in the different inter-delivery interval [Table 4] and month or year of birth.

DISCUSSION

The population of the study comprised of a large proportion of great grand multiparas, mainly religious Jews and Muslims, provided us with a unique opportunity to investigate the question of sex preponderance.

Table 2. Comparison between observed and expected prevalence of families with sequences of same-sex offspring up to nine offspring

Number of same sex sequence	Observed prevalence of families with n same-sex offspring	Total number of families with n offspring	Percent of observed same-sex offspring families	Percent of expected same-sex offspring families*	*P* value
Males					
2	13,409	50,100	26.8%	26.4%	0.07
3	4,703	33,807	13.9%	13.6%	0.07
4	1,410	19,462	7.2%	7.0%	0.14
5	408	10,756	3.8%	3.6%	0.24
6	116	6017	1.9%	1.8%	0.62
7	24	3446	0.7%	0.9%	0.13
8	10	1947	0.5%	0.5%	0.86
9	5	1109	0.5%	0.2%	0.18
Females					
2	11,846	50,100	23.6%	23.6%	0.94
3	4047	33,807	12.0%	11.5%	0.01
4	1151	19,462	5.9%	5.6%	0.04
5	330	10,756	3.1%	2.7%	0.02
6	82	6017	1.4%	1.3%	0.77
7	29	3446	0.8%	0.6%	0.14
8	8	1947	0.4%	0.3%	0.43
9	1	1109	0.1%	0.2%	0.60

*Expected number of males and females was calculated using the reference SRB ratio (1.057) controlling for the same total number of infants

The main finding of this study is that there is no predisposition for same-sex offspring, even in large families with multiple offspring of the same sex. We found a slight natural sex skewing toward males (51% vs. 49%). This observation might be related to the ratio of X and Y bearing sperms. Studies that have investigated the X and Y bearing sperm ratio have shown conflicting results [11,12]. However, more recent studies conducted with the use of fluorescence in situ hybridization technology have shown no difference in the X and Y ratio [13,14]. A large study [15] that used polymerase chain reaction technology to identify the spermatozoa status by amplifying the putative testis determining gene demonstrated a ratio of 51.0% Y- and 49.0% X-bearing spermatozoa. This ratio is identical to the SRB found in ours and other studies evaluating SRB. Interestingly, like our epidemiological observation of the same statistical probability for a boy or a girl in the next-born offspring, even in families with multiple same-sex offspring, a study performed in ejaculates of men with three or more children of the same sex showed no difference in the X-bearing sperm proportion for men with only daughters or Y-bearing sperm proportion for men with only sons. Moreover, several studies have evaluated the relation between sperm count and SRB and demonstrated that morphology and motility are not associated with sex ratio [16,17].

We showed that families with a previous sequence of same-sex offspring have a similar probability to the general population for a boy or a girl is consistent with previous reports. Maconochie and Roman [18], who analyzed all hospital deliveries in Scotland between 1975 and 1988 in families with up to five children, also showed no sex preponderance. They found that SRB appeared to be remarkably robust. There was no evidence to suggest that any naturally occurring factors, including birth order, maternal age, maternal height, paternal or maternal social

Table 3. Comparison between actual and expected sex-ratio at birth in subsequent delivery in boy-only or girl-only families

	Observed subsequent offspring sex			Expected subsequent offspring sex*		
Previous same-sex sequence	**Males**	**Females**	**SRB**	**Males**	**Females**	***P* value**
Males						
1	13,409	12,461	1.076	13,294	12,576	0.153
2	4703	4424	1.063	4690	4437	0.789
3	1410	1337	1.055	1412	1335	0.95
4	408	369	1.106	399	378	0.532
5	116	108	1.074	115	109	0.905
6	24	31	0.774	28	27	0.25
7	10	4	2.5	7	7	0.134
8	5	2	2.5	4	3	0.289
Females						
1	12,384	11,846	1.045	12,451	11,779	0.386
2	4031	4047	0.996	4151	3927	0.007
3	1209	1151	1.05	1213	1147	0.877
4	334	330	1.012	341	323	0.575
5	98	82	1.195	92	88	0.412
6	24	29	0.828	27	26	0.374
7	8	8	1	8	8	0.912
8	2	1	2	2	1	0.596

*Expected number of males and females was calculated by using the reference SRB ratio (1.057) controlling for the same total number of infants.

class, year of delivery, or season of birth, was associated with an alteration in the SRB. Our results oppose the results showed by Garenne [19] who studied sub-Saharan African families with up to 8 sibships and showed that sex ratio varies according to family composition and that there was a gradual increase or decrease in sex ratio (male:female ratio) from first to eighth birth in families with only-boys or only-girls, respectively. In that study the author mentioned that sex heterogeneity found in Africa seems somewhat smaller than elsewhere, and claims narrower heterogeneity in Africa may be genuine, or may be due to more frequent marital changes, which could imply that children of the same mother do not necessarily have the same father. According to that study, overall sex ratios in Africa are very low by international standards. The author summarized that the large differences found in his analysis must be due to some strong underlying factors. Biological factors are the likely candidates to explain the pattern, and in particular the strong asymmetry favoring females.

Some popular theories hypothesized that factors such as vaginal acidity levels or certain diets may have an effect on the sex of the embryo. Although we do not have data to prove those methods, it is likely that parents of multiple same-sex children have tried some or all of the factors. Our findings may imply that those methods are inefficient for sex selection.

Timing of sexual intercourse in relation to ovulation was also proposed as a factor that might have an impact on the sex of the forthcoming embryo. The fact that we did not find a higher prevalence than expected of families with same-sex offspring speaks against the theory of timing of conception.

There are disagreements in the literature regarding the impact of maternal or paternal age on the SRB, with some studies showing no effect, while other favor a minor effect [2,20-22]. The effect of assisted reproductive technology use on sex ratio showed no impact on the overall SRB [23]. As these factors are too weak to explain families of unisexual sibship, we did not include them in the analysis of the SRB. Rather, we assumed maternal parity could serve as a proxy to these factors. When analyzing our data separately for birth order, time interval between births, and year and month of birth, the SRB was consistently similar and did not deviate significantly from the reference SRB.

Over the last few decades, SRB has been skewed in some parts of the world, as a result of male offspring preference, available by the technology of pre-implantation genetic diagnosis (PGD) [24]. Although women who underwent fetus sex selection in a PGD process due to sex-linked inherited diseases could have been included in this study, such cases were extremely rare and would have a minor effect in such a large study population.

Table 4. Comparison between actual and expected sex-ratio at birth in deliveries with inter-delivery interval of 1 to more than 10 years

	Observed			Expected*		
Inter-delivery interval (years)	Males	Females	SRB	Males	Females	*P* value
1	9,899	9,247	1.071	9,839	9,307	0.384
2	19,809	19,180	1.033	20,036	18,953	0.022**
3	10,957	10,470	1.047	11,011	10,416	0.46
4	5537	5146	1.076	5490	5,193	0.361
5	2868	2609	1.099	2815	2,662	0.148
6	1552	1434	1.082	1534	1,452	0.521
7	899	883	1.018	916	866	0.427
8	613	576	1.064	611	578	0.908
9	407	352	1.156	390	369	0.218
10	252	265	0.951	266	251	0.229
more than 10 years	559	536	1.043	563	532	0.823

n=104,050
*Expected number of males and females was calculated by using the reference SRB ratio (1.057) controlling for the same total number of infants.
**Not significant when performing the Bonferroni correction for multiple comparisons (*P* value considered significant when under (0.05/8 = 0.006)
SRB = sex-ratio at birth

Most of our study participants were either Jewish Orthodox or Muslims who normally refrain from induced abortions. Thus, our database accurately represented the naturally occurring SRB. A unique feature in our dataset was the presence of a relatively large number of families with same-sex offspring born to the same mother, which enabled us to examine the popular theory that some women have a natural predisposition toward offspring of the same sex. As the divorce rate among Jerusalem families (both Jews and Muslims) is about 20% [25], the vast majority of offspring of a particular mother were also born to the same father.

LIMITATIONS

One limitation was the exclusion of cases of abortions, intra-uterine fetal deaths and stillbirths, and the exclusion of women who had multiple gestation pregnancies. Another limitation of this study was its retrospective design. However, the strength of this study was the relatively high proportion of grand multiparity in our dataset.

CONCLUSIONS

We did not find evidence for the existence of parents with a natural predilection toward unisexual sibship. The field of sex-ratio at birth remains enigmatic despite numerous studies that were based on very large populations for more than 50 years, with more questions than answers. Research should be aimed at determining biologic factors that govern the selection of a particular sperm over the other in the fertilization process.

Correspondence

Dr. S. Porat
Dept. of Obstetrics and Gynecology, Hebrew University–Hadassah Medical School, Jerusalem 91120, Israel
Fax: (972-2) 677-6489
email: shay.porat@gmail.com

References

1. James WH. The human sex ratio. Part 1: a review of the literature. *Human biol* 1987; 59: 721-52.
2. James WH, Rostron J. Parental age, parity and sex ratio in births in England and Wales, 1968-77. *J Biosoc Sci* 1985; 17: 47-56.
3. Tafuro S, Guilmoto CZ. Skewed sex ratios at birth: a review of global trends. *Early Hum Dev* 2019: 104868.
4. Grant VJ. Maternal personality and sex of infant. *Br J Med Psychol* 1990; 63 (3): 261-6.
5. Masukume G, Grech V. The sex ratio at birth in South Africa increased 9 months after the 2010 FIFA World Cup. *Early Hum Dev* 2015; 91: 807-9.
6. Groeger J, Opler M, Kleinhaus K, et al. Live birth sex ratios and father's geographic origins in Jerusalem, 1964-1976. *Am J Hum Biol* 2017; 29 (3): 10.1002/ajhb.22945.
7. Lyster WR. Altered sex ratio in children of divers. *Lancet* 1982; 2 (8290): 152.
8. Wyatt R, Wilson AM. Children of anaesthetists. *Br Med J* 1973; 1 (5854): 675.
9. James WH. Further evidence that mammalian sex ratios at birth are partially controlled by parental hormone levels around the time of conception. *Hum reprod* 2004; 19: 1250-6.
10. Perret M. Revisiting the Trivers-Willard theory on birth sex ratio bias: role of paternal condition in a Malagasy primate. *PLoS One* 2018; 13: e0209640
11. Bibbins PE, Jr., Lipshultz LI, Ward JB, Jr., Legator MS. Fluorescent body distribution in spermatozoa in the male with exclusively female offspring. *Fertil Steril* 1988; 49: 670-5.
12. Quinlivan WL, Sullivan H. The ratios and separation of X and Y spermatozoa in human semen. *Fertil Steril* 1974; 25: 315-8.
13. Goldman AS, Fomina Z, Knights PA, Hill CJ, Walker AP, Hulten MA. Analysis of the primary sex ratio, sex chromosome aneuploidy and diploidy in human sperm using dual-colour fluorescence in situ hybridisation. *Eur J Hum Genet* 1993; 1: 325-34.
14. Han TL, Ford JH, Webb GC, Flaherty SP, Correll A, Matthews CD. Simultaneous detection of X- and Y-bearing human sperm by double fluorescence in situ hybridization. *Mol Reprod Dev* 1993; 34: 308-13.
15. Cui KH. Size differences between human X and Y spermatozoa and prefertilization diagnosis. *Mol Hum Reprod* 1997; 3: 61-7.
16. Rathje CC, Johnson EEP, Drage D, et al. Differential sperm motility mediates the sex ratio drive shaping mouse sex chromosome evolution. *Curr Biol* 2019; 29: 3692-98.e4.
17. Bae J, Kim S, Chen Z, Eisenberg ML, Buck Louis GM. Human semen quality and the secondary sex ratio. *Asian J Androl* 2017; 19: 374-81.
18. Maconochie N, Roman E. Sex ratios: are there natural variations within the human population? *Br J Obstet Gynaecol* 1997; 104: 1050-3.
19. Garenne M. Sex ratio at birth and family composition in sub-saharan Africa: inter-couple variations. *J Biosoc Sci* 2009; 41: 399-407.
20. Ein-Mor E, Mankuta D, Hochner-Celnikier D, Hurwitz A, Haimov-Kochman R. Sex ratio is remarkably constant. *Fertil Steril* 2010; 93: 1961-5.
21. Jacobsen R, Moller H, Mouritsen A. Natural variation in the human sex ratio. *Hum Reprod* 1999; 14: 3120-5.
22. Takahashi E. The effects of the age of the mother on the sex ratio at birth in Japan. *Ann N Y Acad Sci* 1954; 57: 531-50.
23. Supramaniam PR, Mittal M, Ohuma EO, et al. Secondary sex ratio in assisted reproduction: an analysis of 1,376,454 treatment cycles performed in the UK. *Hum Reprod Open* 2019; (4): hoz020.
24. Chao F, Gerland P, Cook AR, Alkema L. Systematic assessment of the sex ratio at birth for all countries and estimation of national imbalances and regional reference levels. *Proc Natl Acad Sci U S A* 2019; 116: 9303-11.
25. Persons divorcing, by age, sex, and religion. Israeli central bureau of statistics, 2017 [Available from https://old.cbs.gov.il/publications17/1693/pdf/e_print.pdf [Accessed 14 May, 2020].

"An education isn't how much you have committed to memory, or even how much you know. It's being able to differentiate between what you do know and what you don't"

Anatole France (1844–1924), French author, poet, journalist

Freedom is not worth having if it does not include the freedom to make mistakes.

Mahatma Gandhi (1869–1948), Indian political and spiritual leader