Original Article

Firstborn offspring sex ratio is skewed towards female offspring in anesthesia care providers: A questionnaire-based nationwide study from United States

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Abstract

Background: A parental occupation such as anesthesia care provider can involve exposure of the parent to various chemicals in the work environment and has been correlated to skewed offspring sex ratios.
Objectives: The objective was to conduct a nation-wide survey to observe (a) whether firstborn offspring sex ratio (OSR) in anesthesia providers is skewed towards increased female offspring, and (b) to identify potential factors influencing firstborn OSR, particularly those relating to the peri-conceptional practice of inhalational anesthesia induction among anesthesia providers.
Materials and Methods: After institutional review board approval, a questionnaire was uploaded on SurveyMonkey and sent to anesthesia providers through their program coordinators in United States (US) to complete the survey.
Results: The current US national total-population sex ratio is 0.97 male (s)/female with an at-birth sex ratio of 1.05 male (s)/female; comparatively, the results from anesthesia providers' survey respondents ($n = 314$) were a total OSR of 0.93 male (s)/female ($P = 0.61$) with firstborn OSR 0.82 male (s)/female (a 6% increase in female offspring; $P = 0.03$), respectively. The only significant peri-conceptional factor related to anesthesia providers' firstborn OSR's skew was inhalational induction practice by anesthesia care provider favoring female offspring ($P < 0.01$).
Conclusion: Based on the results of this limited survey, it can be concluded that anesthesia care providers who practice inhalation induction of anesthesia during the peri-conceptional period are significantly more likely to have firstborn female offspring.

Key words: Anesthesia care providers, inhalational induction of anesthesia, offspring sex ratio, parental occupation, peri-conceptional factors

Introduction

Sex ratio is defined as the ratio of males to females in a population. A parental occupation such as anesthesia care provider can involve exposure of the parent to various chemicals in the work environment and has been correlated to skewed offspring sex ratios (OSR) favoring higher proportions of female offspring.[1] However, reported studies in anesthesiologists related to anesthesia practice and its effects on pregnancy including OSR were performed in the early 1970s and were based on small sample populations.[1-6] In addition to the documentation of higher risks for miscarriages, stillbirths, and fetal malformations in female anesthesia care providers, these studies that were performed before the advent of scavenger systems for anesthesia circuits (late 1970s - early 1980s[7]) had documented higher proportions of female offspring in male anesthesia care providers, secondary to occupational exposure to inhalational anesthetics.[2-5] With scavenger systems becoming standard of care for anesthesia care delivery environments in United States over the last three decades, it is valid to investigate whether these earlier reported effects are still evident in the current anesthesia care provider population. As scavenger systems for anesthesia circuits are largely ineffective to protect against occupational exposure to high concentrations of inhalational anesthetics during inhalational induction of anesthesia, an aim of the current study was to observe whether earlier reported effects might be dependent on the type of anesthesia induction.

The present study was designed to investigate firstborn OSR in anesthesia providers and potential factors influencing

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firstborn OSR. Other effects of occupational exposure to inhalational anesthetics such as incidence of miscarriages and fetal malformations were not investigated. To avoid an overly long questionnaire, only details regarding firstborn offspring were sought from the respondents. Therefore, the primary objectives of this current study were to conduct a nation-wide survey to observe (a) whether firstborn OSR in anesthesia providers is skewed towards female offspring and if so, (b) to identify potential factors influencing firstborn OSR, particularly related to the peri-conceptional practice of inhalational induction (INH) of anesthesia among anesthesia providers.

Materials and Methods

After institutional review board approval, a questionnaire (Appendix A) was uploaded on SurveyMonkey[8] and sent to anesthesia providers (anesthesiology residents/fellows, anesthesiologists, student registered nurse anesthetists, and certified registered nurse anesthetists) through their anesthesiology residency/fellowship program coordinators and nurse anesthetists' program coordinators in United States (US). Survey respondents were asked to complete the survey to assess OSR

- Among respondents' biological children that were born without assisted reproductive technology (total OSR) and
- Among respondents' firstborn children (firstborn OSR)

Additionally, peri-conceptional factors known to confound OSRs were surveyed only for firstborn offspring:

- Practice of INH
- Operating room environment (with and without anesthesia scavenging systems)
- Smoking
- Heavy alcohol use
- Obesity and nutritional supplements
- Exogenous hormones use (birth control pills and fertility agents)
- Physical stress in terms of work hours per week

Statistical analysis

Statistical analysis required ANOVA or *t*-test where appropriate for continuous data and Chi-squared tests for categorical data. Logistic regression analysis was performed on confounding factors to assess their predictive effect on firstborn OSR. Results were considered significant at a level of $P < 0.05$.

Results

The response rate to the survey provided a total of 443 respondents [Figure 1], of which 314 respondents were found to be eligible for survey analysis [Figure 2]. The data results from eligible responses' analysis showed that compared to the US total-population sex ratio of 0.97 male (s)/female,[9,10] the total OSR for survey respondents was 0.93 male (s)/female (power 1-$\beta > 0.99$; $P = 0.61$). As compared to US at-birth sex ratio of 1.05 male (s)/female,[11] firstborn OSR from the survey was 0.82 male (s)/female (a 6% increase in female offspring; power 1-$\beta = 0.61$; $P = 0.03$). The abovementioned survey data-derived OSRs were statistically compared to general population data based on the statistical methods as applied by Wyatt and Wilson.[5]

Male respondents' age (paternal age) at the time of conception of firstborn child was not significantly different (29 ± 5 years if firstborn offspring was male; 30.05 ± 5.09 years if firstborn offspring was female; $P = 0.21$); however, female respondents' age (maternal age) at the time of conception of firstborn

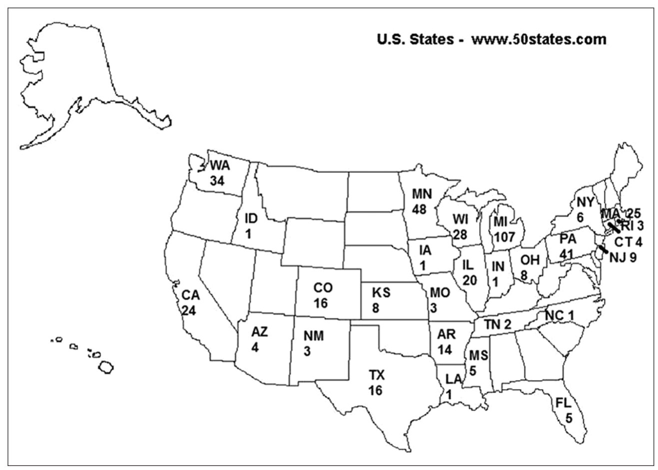

Figure 1: Responders' Numbers depending on their State of Origin across the United States (adapted from free blank U.S. States Map available at www.50states.com)

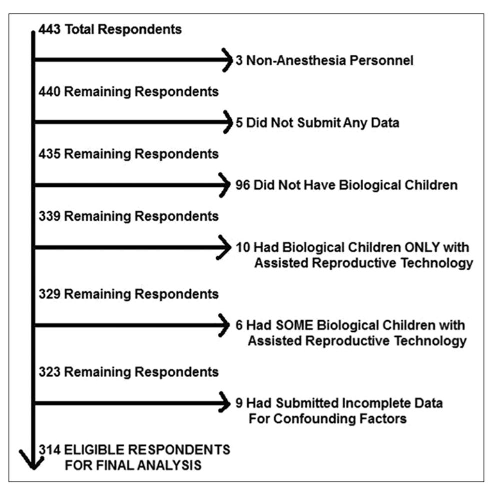

Figure 2: Distribution of respondents to deduce the final eligible respondents for comparative analysis

child was significantly lower if their firstborn offspring were males (28.51 ± 4.3 years versus 30.27 ± 4.3 years; $P = 0.01$). Logistic regression analysis observed that other significant peri-conceptional confounding factors for firstborn OSR included INH practice by respondents (OSR 0.41 male (s)/female instead of 0.91 male (s)/female; power 1-β = 0.70; $P = 0.02$) and smoking by respondents (OSR 2.12 male (s)/female instead of 0.75 male (s)/female; power 1-β = 0.68; $P = 0.02$). None of the other surveyed factors significantly affected firstborn OSR; even absence of anesthesia gas scavenging systems in operating rooms did not affect firstborn OSR significantly [Tables 1 and 2]. After combining the respondents and their spouses for sub-group analysis of male/female anesthesia providers and male/female smokers, smoking's effect on firstborn OSR disappeared ($P = 0.02$ changed to $P = 0.08$) and INH practice's effect on firstborn OSR accentuated ($P = 0.02$ changed to $P = 0.009$) after correction for parental sex [Table 3]. At time of conception of their firstborn child, the duration of cumulative occupational exposure to waste anesthetic gases was not significantly different among

Table 1: Peri-conceptional confounding factors for firstborn offspring sex ratio (OSR) among survey responders

Factor	OSR if factor was absent [male (s)/female]	OSR if factor was present [male (s)/female]	Power (1-β)	*P*-value (*significant if *P*<0.05)
Operating room (OR) working	1.00	0.74	0.27	0.23
Inhalation induction practice	0.91	0.41	0.70	0.02*
Anesthesia-gas scavenging systems in OR	1.17	0.77	0.22	0.24
Abnormal nutritional status	0.82	0.77	0.03	0.87
Smoking	0.75	2.12	0.68	0.02*
Heavy alcohol use	0.81	2	0.10	0.59
Birth control pills use	0.79	1.5	0.23	0.29
Fertility agents use	0.82	0.67	0.04	>0.99
Nutritional supplement use	0.84	0.70	0.09	0.65
More than 40 work-hours per week	1.05	0.79	0.13	0.40

OSR=Offspring sex ratio

Table 2: Peri-conceptional confounding factors for firstborn offspring sex ratio (osr) among survey responders' spouses

Factor	OSR if factor was absent [male (s)/female]	OSR if factor was present [male (s)/female]	Power (1-β)	*P*-value (*significant if *P*<0.05)
Operating room (OR) working	0.86	0.50	0.29	0.20
Inhalation induction practice	0.82	0.75	0.03	>0.99
Anesthesia-gas scavenging systems in OR	0.84	0.67	0.10	0.59
Abnormal nutritional status	0.80	0.93	0.05	0.70
Smoking	0.78	1.25	0.22	0.31
Heavy alcohol use	0.83	0.2	0.23	0.23
Birth control pills use	0.80	1.14	0.09	0.60
Fertility agents use	0.79	5.00	0.47	0.09
Nutritional supplement use	0.85	0.47	0.23	0.27
More than 40 work-hours per week	0.96	0.76	0.16	0.39

OSR=Offspring sex ratio

Table 3: Sub-group analysis of significant peri-conceptional factors corrected for parental sex to elicit effect's significance on offspring sex ratio

Parents' peri-conceptional characteristic (*n*)	Firstborn offspring was male	Firstborn offspring was female	*P*-value (*significant if *P*<0.05)
Both parents practiced inhalational induction	3	1	0.009*
Father practiced inhalational induction	4	13	
Mother practiced inhalational induction	7	23	
None of the parents practiced inhalational induction	127	136	
Both parents smoked	7	4	0.08
Father smoked	9	9	
Mother smoked	9	3	
None of the parents smoked	116	157	

anesthesia care providers (3.4 ± 5.8 years for male offspring; 3.8 ± 4.8 years for female offspring; $P = 0.26$).

Discussion

The results of this survey raise potential occupational safety concerns regarding the influence of INH on OSR. INH is the standard of care, especially for pediatric anesthesia work environments. Anesthesia care providers practicing INH can be exposed to high concentrations of waste anesthesia gas exposure.[12,13] This occupational exposure can be affected by differing techniques of INH such as conventional stepwise INH or vital capacity rapid INH.[14,15] Another factor affecting occupation exposure to anesthetic gasses may be the scavenging or extraction methods of the waste anesthesia gases.[16-18]

The viability of male-sex determining Y-bearing sperms[19] may be affected by occupational exposure to waste anesthetic gases that may affect OSR in anesthesia care providers[1] (both male providers as well as female providers). Such effects could occur from anesthetic exposure affecting Y-bearing spermatozoa in paternal genital tract (pre-coital life cycle of sperm) as well as in maternal genital tract (post-coital life cycle of sperm). However, spermatozoa functionality tests following occupational exposure to anesthetics have been sparsely investigated.[1] Other peri-conceptional factors that may alter OSR include parental exposure to smoking,[20-22] alcohol abuse,[23-26] stress,[27] obesity,[28] or the use of hormones (exogeneous or endogeneous).[29]

The present survey was designed so that anesthesia providers could compare the anesthesia care provider community's OSR (total OSR) with the total-population sex ratio in US. However, their firstborn OSR was compared with at-birth sex ratio in US. OSR for the firstborn offspring only (and not for each offspring) was used as the primary outcome because it was the authors' view that such intricate details regarding OSR-related peri-conceptional confounding factors would be best remembered by the parents for their firstborn children; and limiting the investigation to firstborn OSR would exclude the potential peri-conceptional confounding factor of cumulative occupational exposure to inhalational anesthetics for later-born OSR. Moreover, it was the authors' view that questionnaire process would be overly long if OSR-related peri-conceptional confounding factors had to be assessed for each offspring.

As the significant findings (INH practice) for the firstborn OSR were adequately powered ($1\text{-}\beta = 0.70$), these results may instigate future studies to investigate effects of INH practice on the later-born OSR. As the absence of anesthesia gas scavenging systems in operating rooms was insignificant but underpowered (power $1\text{-}\beta = 0.22$; $P = 0.24$) confounding factor, the survey results suggest that the leakage around the face-mask during INH practice and consequent exposure to transient but high concentrations of inhalational anesthetics may be the primary underlying mechanism for firstborn OSR's skew. Scavenging systems attached to anesthesia machines are primarily efficient in maintaining the operating room environments during maintenance of inhalational anesthesia but are largely ineffective to protect against occupational exposure at the time of inhalational induction of anesthesia. The accentuation of the significance after correction for parental sex ($P = 0.009$ vs. $P = 0.02$) even though the cumulative occupational exposure years were insignificantly different ($P = 0.26$) at the time of first conceptions in anesthesia providers (both male as well as female providers) suggest acute (not chronic) effects of waste anesthetic gases on firstborn OSR [Table 3]. Moreover, maternal genital tract's role in determining firstborn OSR may be related to maternal age (a potential confounding factor) because per our limited results, older female anesthesia care providers more often bore firstborn female offspring. However, these observations need validation in a larger survey sample population to confirm whether these effects on OSR are secondary to direct effects of waste anesthetic gases and/or immunological changes against Y-bearing sperms induced by exposure to waste anesthetic gases. Additionally, the future studies may need to further elicit whether

- OSR's skew is related to effects on the germ cells and/or sperms if the OSR's skew is secondary to only male anesthesia care providers' occupational exposure, or
- OSR's skew is related to Y-bearing sperms failing to fertilize as many ova as X-bearing sperms and/or male zygotes failing to implant and/or survive as term fetus if the OSR's skew is secondary to only female anesthesia care providers' occupational exposure.

There were some limitations to the present study.

- Not surveying for the age of respondents' spouses during their firstborn children's peri-conceptional period meant that assessment of parental age as confounding factor could not be analyzed.
- Questions could have been framed more clearly to prevent the responders from submitting data related to their children born with assisted reproductive technology [Figure 2].
- Despite the adequate statistical power for INH practice's effect on OSR's skew, effects of other peri-conceptional confounding factors could have been underestimated due to the lack of statistical power [Tables 1 and 2].
- To validate and extend the results of this present study that focused on firstborn offspring, a larger number of surveyed anesthesia care providers will be

required in future studies with additional focus on peri-conceptional factors related to every offspring born to anesthesia care providers irrespective of their birth order. A larger number based future study should also interpret our results for the four couples wherein both parents practiced inhalational induction during peri-conceptional period.

Conclusion

Based on the results of this limited survey, it can be concluded that anesthesia care providers who practice inhalation induction of anesthesia during the peri-conceptional period are significantly more likely to have firstborn female offspring.

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Appendix A

Anesthesia Providers have more Baby Girls than Baby Boys: Myth or Fact?

1. Are you an Anesthesia Provider (MD or DO Anesthesiologist/ Anesthesiology Resident/Fellow/CRNA/SRNA)?
   a. Yes
   b. No =====
2. Which state do you presently practice?
   a. Name of State
3. Which year did you first start practicing in the operating room as anesthesia resident/student?
   a. 19--/20--
4. Which of the following best describes you NOW?
   a. Pediatric Anesthesiologist
   b. Non-Pediatric Anesthesiologist
   c. Pediatric Anesthesiology Fellow
   d. Non-Pediatric Anesthesiology Fellow
   e. CA-3
   f. CA-2
   g. CA-1
   h. PGY-1 (Anesthesiology) and AMG
   i. PGY-1 (Anesthesiology) and IMG with no prior Anesthesia Experience
   j. PGY-1 (Anesthesiology) and IMG with prior Anesthesia Experience
   k. Pediatric CRNA
   l. Non-Pediatric CRNA
   m. SRNA
5. What is your sex?
   a. Male
   b. Female
6. Which of the following best describes your spouse?
   a. Pediatric Anesthesiologist
   b. Non-Pediatric Anesthesiologist
   c. Pediatric Anesthesiology Fellow
   d. Non-Pediatric Anesthesiology Fellow
   e. CA-3
   f. CA-2
   g. CA-1
   h. PGY-1 (Anesthesiology) and AMG
   i. PGY-1 (Anesthesiology) and IMG with no prior Anesthesia Experience
   j. PGY-1 (Anesthesiology) and IMG with prior Anesthesia Experience
   k. Pediatric CRNA
   l. Non-Pediatric CRNA
   m. SRNA
   n. None of the above
7. How often do you practice inhalation induction of anesthesia for your patients?
   a. Never
   b. Rarely (<20% of patients)
   c. Sometimes (20-50% of patients)
   d. Often (50-80% of patients)
   e. Almost always (>80% of patients)
   f. Always
8. How often does your spouse practice inhalation induction of anesthesia for his/her patients?
   a. Never
   b. Rarely (<20% of patients)
   c. Sometimes (20-50% of patients)
   d. Often (50-80% of patients)
   e. Almost always (>80% of patients)
   f. Always
   g. Not applicable
9. Do you have biological children?
   a Yes
   b. No =====
10. How many biological children do you have without assisted reproductive technology?
    a. Number
    b. None =====
11. How many daughters do you have?
    a. Number
12. How many sons do you have?
    a. Number
13. What is the sex of your firstborn child?
    a. Male
    b. Female
14. In which month was your first child born?

a. January
b. February
c. March
d. April
e. May
f. June
g. July
h. August
i. September
j. October
k. November
l. December

15. What was your age at the time of conception (8-10 months prior to birth) of your first child?
    a. Number in years
16. Around the time of conception of your firstborn child, were you still working in the operating room?
    a. Yes
    b. No
17. Around the time of conception of your firstborn child, was your spouse working in the operating room?
    a. Yes
    b. No
    c. Not Applicable
18. At the time of conception of your firstborn child, how many years of occupational exposure to anesthesia environment did you have?
    a. Years of anesthesia practice
19. At the time of conception of your firstborn child, how many years of occupational exposure to anesthesia environment did your spouse have?
    a. Years of anesthesia practice
    b. Not Applicable
20. Around the time of conception of your firstborn child, how often were you practicing inhalation induction of anesthesia for your patients?
    a. Never
    b. Rarely (<20% of patients)
    c. Sometimes (20-50% of patients)
    d. Often (50-80% of patients)
    e. Almost always (>80% of patients)
    f. Always
21. Around the time of conception of your firstborn child, how often was your spouse practicing inhalation induction of anesthesia for his/her patients?
    a. Never
    b. Rarely (<20% of patients)
    c. Sometimes (20-50% of patients)
    d. Often (50-80% of patients)
    e. Almost always (>80% of patients)
    f. Always
    g. Not Applicable
22. Around the time of conception of your firstborn child, were scavenging systems available in your operating rooms?
    a. Yes
    b. No
23. Around the time of conception of your firstborn child, were scavenging systems available in your spouse's operating rooms?
    a. Yes
    b. No
    c. Not Applicable
24. Around the time of conception of your firstborn child, how will you define your nutritional status?
    a. Normal
    b. Underweight
    c. Overweight
    d. Obese
25. Around the time of conception of your firstborn child, how will you define your spouse's nutritional status?
    a. Normal
    b. Underweight
    c. Overweight
    d. Obese
26. Around the time of conception of your firstborn child, were you smoking?
    a. Yes
    b. No
27. Around the time of conception of your firstborn child, was your spouse smoking?
    a. Yes
    b. No
28. Around the time of conception of your firstborn child, were you a heavy* user of alcohol (*Definition of heavy use: Men- Over 5-6 drink equivalents per day; Women- Over 3-4 drink equivalents per day)
    a. Yes
    b. No
29. Around the time of conception of your firstborn child, was your spouse a heavy* user of alcohol. (*Definition of heavy use: Men- Over 5-6 drink equivalents per day; Women- Over 3-4 drink equivalents per day)
    a. Yes
    b. No
30. Around the time of conception of your firstborn child, were you using birth control pills?
    a. Yes
    b. No
    c. Not Applicable
31. Around the time of conception of your firstborn child, was your spouse using birth control pills?
    a. Yes
    b. No
    c. Not Applicable
32. Around the time of conception of your firstborn child, were you using fertility agents?
    a. Yes
    b. No
    c. Not Applicable
33. Around the time of conception of your firstborn child, was your spouse using fertility agents?
    a. Yes
    b. No
    c. Not Applicable
34. Around the time of conception of your firstborn child, were you using nutritional (nutraceutical) supplements?
    a. Yes
    b. No

35. Around the time of conception of your firstborn child, was your spouse using nutritional (nutraceutical) supplements?
    a. Yes
    b. No
36. Around the time of conception of your firstborn child, what were your work-hours?
    a. <40 hrs a week
    b. 40-80 hrs a week
    c. >80 hrs a week
37. Around the time of conception of your firstborn child, what were your spouse's work-hours?
    a. <40 hrs a week
    b. 40-80 hrs a week
    c. >80 hrs a week

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