Does the Mother or Father Determine the Offspring Sex Ratio? Investigating the Relationship between Maternal Digit Ratio and Offspring Sex Ratio

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Abstract

Objective

In mammals, high parental testosterone levels present around the time of conception are thought to skew offspring sex ratio toward sons. The second to fourth digit ratio (digit ratio) is now widely accepted as a negative correlate of prenatal testosterone. Thus, we investigated the association between digit ratio and offspring sex ratio.

Methods

A total of 508 Korean patients (257 males and 251 females) less than 60 years old who had one or more offspring were prospectively enrolled. The lengths of the 2nd and 4th digits of the right hand were measured by a single investigator using a digital vernier calliper. Next, the patients’ lifetime offspring birth sex ratios were investigated.

Results

Maternal (rather than paternal) digit ratio was significantly associated with the number of sons ($r = -0.153$, $p = 0.015$), number of daughters ($r = 0.130$, $p = 0.039$), and offspring sex ratio ($r = -0.171$, $p = 0.007$). And, the maternal digit ratio was a significant factor for predicting offspring sex ratio ($B = -1.620$, $p = 0.008$) on multiple linear regression analysis. The female patients with a lower digit ratio ($<0.95$) were found to have a higher offspring sex ratio (0.609 versus 0.521, $p = 0.046$) compared to those with a higher digit ratio ($\geq 0.95$). Furthermore, females in the low digit ratio group have a probability 1.138 greater of having sons than females in the high digit ratio group.

Conclusions

Maternal digit ratio was negatively associated with offspring sex ratio. Females with a lower digit ratio were more likely to have more male offspring compared to those with a higher
digit ratio. Thus, our results suggest that the sex of offspring might be more influenced by maternal rather than paternal factors.

Introduction

The second to fourth digit ratio (digit ratio) is known to be sexually dimorphic; females have larger digit ratios than males [1–4]. This ratio is primarily determined during fetal development [5–8] and changes little after sexual maturation [8]. This gender-associated difference may be influenced by changes in prenatal steroid concentrations [1,5]. Prenatal testosterone concentrations have been demonstrated to cause sex differences in digit ratio [9,10]. The direction of change of the digit ratio depends on the gestational timing and duration of fetal testosterone exposure [9,10]. Thus, digit ratio is now widely accepted as a negative correlate of prenatal testosterone around about the end of the first trimester [1,5,11,12].

However, there is no simple understanding of fetal testosterone exposure from determining adult digit ratio. Hollier et al. [13] reported that adult digit ratio is not related to umbilical cord androgens or estrogens concentrations at late gestation. Furthermore, there is probably not a strong correlation between digit ratio and adult testosterone levels. However, the waist-to-hip ratio (WHR) in women is positively correlated with serum levels of testosterone and negatively with women’s digit ratio. Furthermore, the WHR of mothers has been reported to correlate negatively with the digit ratio of their children [14]. This suggests that women with genes for high testosterone have children with low digit ratio.

In mammals, high parental testosterone levels present during conception have been proposed to skew the offspring sex ratio toward sons [15,16]. In addition to circulating testosterone concentration, high maternal estrogen levels have been reported to correlate with female-biased offspring sex ratios among gray mouse lemurs [17]. To date, there are three papers that have examined links between digit ratio and offspring sex ratio. Manning et al. reported that both men and women with lower digit ratios had significantly higher offspring sex ratios (i.e., more male offspring) in a large (n = 456) cross-cultural study (Spanish, English, and Jamaican) [18]. This paper was followed by that of Helle and Lilley who reported that in a sample of Finnish women, maternal digit ratio could not predict lifetime offspring sex ratios [19]. However, Ventura et al. reported digit ratio data from 106 mothers and their children and found mothers with low digit ratio tended to have sons [20].

Up to this point, data indicating the relationship between digit ratio and offspring sex ratio are inconsistent and controversial. Therefore, the purpose of the present study was to investigate the association between digit ratio and offspring sex ratio.

Materials and Methods

Study participant selection

Of the patients that were hospitalized for urological surgery at a single tertiary academic center, a total of 508 (257 males and 251 females) Korean patients less than 60 years old who had one or more offspring were prospectively enrolled in the study. Ethical approval (approval number: GBIRB2013-88) was obtained from the Institutional Review Board (IRB) of Gachon University Gil Hospital (Incheon, Republic of Korea). All participants signed an informed consent. Patients with a history of induced abortion that artificially affected the offspring sex ratio were excluded. In addition, patients with a history of arthritis (e.g., rheumatoid arthritis), as well as those who had fingers amputated, were excluded.
Digit measurement
Before assessing the patients’ offspring, the 2nd and 4th digits of the right hand were directly measured by a single investigator using a digital vernier calliper accurate to 0.01 mm. Digit length of right hand was measured on the ventral surface of the hand from the basal crease of the digit to the fingertip [1]. To standardize keeping the fingers similarly straight during measurements, fingers and hands were placed on a flat hard surface of desk. In order to reduce errors in measurement, the mean of two digit ratios calculated based on duplicate measurements were used for the analysis. For assessing repeatability of two measurements, we used the method proposed by Bland and Altman [21]. The average of differences between two digit ratios calculated based on duplicate measurements using a digital vernier calliper by a single investigator is -0.001. The standard deviation of differences between the 508 pairs of repeated measurements is 0.013. The coefficient of repeatability is twice this, or 0.026 for digital vernier caliper (Mean - 2SD = -0.027; Mean + 2SD = 0.025). This suggests that a direct measurement of digit ratio using a digital vernier calliper has acceptable repeatability [21].

Investigation of the offspring sex ratio
Information about the patients’ lifetime offspring birth sex ratio was collected. For the present study, we defined offspring sex ratio as the proportion of sons to total offspring (offspring sex ratio = number of sons / number of total offspring).

Statistical analysis
Relationships between study variables were analyzed using Pearson’s linear correlation. To identify significant predictive factors that influenced the offspring sex ratio, multiple linear regression analyses were performed. Student’s t-test and relative risk (RR) analysis were used to compare variables for the two study groups arranged according to digit ratio. To compare the offspring sex ratios between three groups arranged according to the number of total offspring, one-way analysis of variance (ANOVA) with post hoc Bonferroni test was used. Analyses were performed using SPSS 12.0 (SPSS, Chicago, IL, USA) and p-values less than 0.05 were considered statistically significant.

Results
Participant characteristics
The mean and median age of all subjects were 50.1 and 51.0 (range: 30.0–59.0), respectively. The mean and median number of total offspring of all 508 patients were 1.94 and 2.00 (range: 1–6), respectively. The median digit ratios of males, females, and all subjects were comparable 0.947 (range: 0.831–1.061), 0.952 (range: 0.791–1.123), and 0.947 (range: 0.791–1.123), respectively. The characteristics of all 508 patients are summarized in Table 1.

Correlation study
Among the different variables evaluated, a correlation analysis (Table 2) showed that the maternal digit ratio was significantly associated with the number of sons (r = -0.153, p = 0.015), number of daughters (r = 0.130, p = 0.039), and offspring sex ratio (r = -0.171, p = 0.007) (Figs 1–3). In contrast, male digit ratio was not correlated with the number of sons, number of daughters, or offspring sex ratio (Table 2). Results of multiple linear regression analysis (Table 3) demonstrated that the maternal digit ratio was a significant factor for predicting offspring sex ratio (B = -1.620, p = 0.008).
Comparison study

The mean and median values of digit ratios of males, females, and all the patients were very close to 0.95 (Table 1). Therefore, we divided all the patients into two groups according to digit ratio cutoff of 0.95 (digit ratio < 0.95 versus digit ratio ≥ 0.95). The offspring sex ratio and proportion of patients with one or more sons (number of sons ≥ 1) among male participants were not different between the two study groups (Table 4). However, female patients in the lower digit ratio group were found to have a higher offspring sex ratio (0.609 versus 0.521, p = 0.046) and a greater proportion of individuals with one or more sons (number of sons ≥ 1) (88.4% versus 77.7%, p = 0.023) compared to those in the higher digit ratio group (Table 4).

Relative risk analysis

In females, the relative risk (RR) of having one or more sons in the group with digit ratio < 0.95, as compared to the ≥ 0.95 group, is 1.138, and this RR is statistically significant (95% CI: 1.017–1.274). In other words, females in the low digit ratio group have a probability 1.138 greater of having sons than females in the high digit ratio group. In males, the RR of having sons in the low digit ratio group, as compared to the high digit ratio group, is 0.948, and this RR is not statistically significant (95% CI: 0.830–1.082) (Table 5).

Sub-group analysis of 394 patients with two or more children

Of 508 patients, 77.6% (394/508) have two or more children. Table 6 shows that offspring sex ratio decreases as the number of total offspring increases (Table 6). The results on Pearson’s linear correlation analysis and multiple linear regression analysis of 394 patients with two or more children are similar to those of total 508 patients (Tables 7 and 8).

Discussion

Mammals usually produce approximately equal numbers of sons and daughters. For years, the belief has been that mammalian sex is randomly determined according to whether an X- or

Table 1. Characteristics of the study population.

|                      | Total      | Males      | Females    | p-value* |
|----------------------|------------|------------|------------|----------|
| N                    | 508        | 257        | 251        |          |
| Age (yrs)            | 50.1 ± 6.7 | 50.1 ± 7.2 | 50.0 ± 6.2 | 0.928    |
| Height (cm)          | 164.2 ± 8.5| 170.6 ± 5.9| 157.7 ± 5.3| <0.001   |
| Weight (kg)          | 65.1 ± 11.0| 70.7 ± 10.4| 59.3 ± 8.4 | <0.001   |
| BMI (kg/m²)          | 24.1 ± 3.2 | 24.2 ± 3.1 | 23.9 ± 3.2 | 0.163    |
| Second digit length (cm) | 6.821 ± 0.46 | 7.039 ± 0.399 | 6.597 ± 0.418 | <0.001 |
| Fourth digit length (cm) | 7.189 ± 0.498 | 7.436 ± 0.423 | 6.936 ± 0.439 | <0.001   |
| Digit ratio          | 0.949 ± 0.033| 0.947 ± 0.030| 0.952 ± 0.037| 0.112    |
| Number of total offspring | 1.94 ± 0.69 | 1.89 ± 0.67 | 2.00 ± 0.72 | 0.077    |
| Number of sons       | 1.04 ± 0.71 | 1.00 ± 0.71 | 1.08 ± 0.70 | 0.182    |
| Number of daughters  | 0.90 ± 0.79 | 0.89 ± 0.77 | 0.92 ± 0.80 | 0.717    |
| Offspring sex ratio  | 0.556 ± 0.364| 0.549 ± 0.379| 0.564 ± 0.349| 0.656    |
| Proportion of patients with only sons without any daughters (%) | 32.9 (167/508) | 34.2 (88/257) | 31.5 (79/251) | 0.508    |
| Proportion of patients with one or more sons (%) | 79.9 (406/508) | 77.0 (198/257) | 82.9 (208/251) | 0.101    |

BMI, body mass index; Digit ratio, 2nd digit length / 4th digit length.
*p-value between males vs females.

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Y-chromosome-bearing spermatozoon fertilizes the oocyte. However, this belief is now being challenged by increasing evidence from field (evolutionary biologic investigations), laboratory, and clinical studies suggesting that mammalian mothers may have a decisive influence on their offspring’s sex. Additionally, researchers have suggested that ‘maternal good condition’ [22,23] and ‘maternal dominance’ [24] are related to the conception of male offspring.

### Good condition and diet

Since Trivers and Willard [22] proposed the good condition hypothesis in 1973, evolutionary biologists have found that a better maternal physical condition was significantly related to higher offspring sex ratios (i.e., more male offspring) [23]. Those choosing the good condition...
hypothesis looked for links in the studies of diet [25–28], and, more clearly, unsaturated fats [29], polyunsaturated fatty acids [30,31], and glucose [32].

More recently, experimental studies have demonstrated the crucial influence of pre-conceptual maternal diet on the offspring sex ratio [26,29–31,33]. A diet very high in saturated fat causes female mice to have significantly more sons than either control or insufficient fat diet females [29]. However, male mice fed similar diets (i.e., a diet very high in saturated fat) had neither more Y-chromosome-bearing sperm nor sired more male offspring than female offspring [29]. These findings suggested that the effects of diet were ‘apparent exclusively in the female’ [29]. Furthermore, a diet enriched with polyunsaturated fatty acids caused ewes to bear more male offspring [31], and a large study showed that pre-conception diet had a similar effect in humans [28].
High maternal glucose levels induced via diet before conception (pre-conceptual diets) differentially promote the development of male embryos post-conception [32,34]. Additionally, increased glucose levels in the post-conceptual uterine environment are related to the preferential development of male embryos [27,32]. These findings coincide with those from an earlier study by reproductive biologists who demonstrated that male embryos grow more rapidly than female embryos [35–39].

In humans, positive correlations also exist between maternal nutritional state and offspring sex ratio [40–44]. Recently, it has been suggested that a change in condition, rather than the maternal body condition per se, may be a better predictor of offspring’s sex. In other words, mothers getting an improvement in condition at the time of conception were more likely to give birth to males [15,22,45–48].
Maternal dominance and testosterone

Most studies about maternal dominance demonstrated that more dominant females than other females in the same group are more likely to bear male offspring [23,40,49–51]. Recognizing that a tendency to dominant behavior is underpinned by testosterone [52–54], researchers who preferred the maternal dominance hypothesis sought a connection between pre-conceptual maternal testosterone concentration and offspring sex ratio [55–59]. Independently, they found that higher pre-conceptual maternal testosterone levels measured in feces [55], serum [56], and follicular fluid [57–59] were significantly associated with higher offspring sex ratios (i.e., more males than females). However, Helle et al. [56] found that paternal testosterone concentration was not associated with offspring sex ratios.
### Table 3. Relationship between offspring sex ratio and study variables according to multiple linear regression analysis.

|         | B     | p-value |
|---------|-------|---------|
| **Males** |       |         |
| Age (yrs) | 0.001 | 0.663   |
| Height (cm) | 0.900 | 0.917   |
| Weight (kg) | -0.004 | 0.143   |
| Digit ratio | 1.302 | 0.101   |
| **Females** |       |         |
| Age (yrs) | -0.001 | 0.809   |
| Height (cm) | 0.000 | 0.962   |
| Weight (kg) | 0.001 | 0.659   |
| Digit ratio | -1.620 | 0.008   |

Multiple linear regression analyses were performed. Digit ratio, 2nd digit length / 4th digit length.

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### Table 4. Comparisons of variables between the two study groups arranged according to digit ratio.

|         | Males | Females |
|---------|-------|---------|
| **Age (yrs)** | 141 | 121 |
| **Height (cm)** | 49.8 ± 7.7 | 50.4 ± 6.7 |
| **Weight (kg)** | 170.3 ± 5.8 | 170.3 ± 6.0 |
| **BMI (kg/m²)** | 69.9 ± 10.0 | 71.6 ± 10.7 |
| **Digit ratio** | 23.9 ± 3.0 | 24.6 ± 3.2 |
| **Second digit length (cm)** | 6.976 ± 0.335 | 7.116 ± 0.455 |
| **Fourth digit length (cm)** | 7.531 ± 0.359 | 7.321 ± 0.466 |
| **Digit ratio** | 0.926 ± 0.021 | 0.972 ± 0.018 |
| **Number of total offspring** | 1.89 ± 0.65 | 1.88 ± 0.69 |
| **Number of sons** | 0.95 ± 0.71 | 1.05 ± 0.71 |
| **Number of daughters** | 0.94 ± 0.76 | 0.83 ± 0.78 |
| **Offspring sex ratio** | 0.525 ± 0.378 | 0.579 ± 0.380 |
| **Proportion of patients with only sons without any daughters (%)** | 31.2 (44/141) | 37.9 (44/116) |
| **Proportion of patients with one or more sons (%)** | 75.2 (106/141) | 79.3 (92/116) |

Student's t-test was used to compare variables between the two study groups arranged according to digit ratio. BMI, body mass index; DR, digit ratio (2nd digit length / 4th digit length).

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Grant et al. [58] and Garcia-Herreros et al. [59] demonstrated that the sex of bovine embryos produced by in vitro fertilization (IVF) may be related to the maternal preovulatory follicular testosterone levels, indicating that oocytes developing in high testosterone concentrations are more likely to be fertilized by Y-chromosome-bearing spermatozoa [33]. These findings [57,58] suggest that there may be a crucial time during the development of the zona pellucida, and that the molecular composition of the zona pellucida may be delicately influenced by high levels of follicular testosterone which make the oocyte more inclined to be fertilized by a Y-chromosome-bearing spermatozoon [33].

Digit ratio and offspring sex ratio

One of the novel findings of the present study was that maternal (but not paternal) digit ratio was negatively associated with offspring sex ratio. And, females with a lower digit ratio were found to have a higher offspring sex ratio compared to those with a higher digit ratio. This means that the sex of offspring might be more influenced by maternal rather than paternal factors. In other words, the association of offspring sex ratio to maternal digit ratio may indicate linkage with unknown genetic traits, gestational environment or other factors related more to the mother rather than the father.

Actually, in the present study, the Pearson correlation coefficient between maternal digit ratio and offspring sex ratio was -0.171 (r = -0.171, p = 0.007), which means weak negative correlation. However, although the determination coefficient (R²) is very low (R² = 0.030), digit ratio still remained significant after multiple linear regression analysis in females, but not in males. In other words, the significant relationship between digit ratio and offspring sex ratio appears in females but not in males. We think that this is more important in the present study.

Table 5. Comparison of the probability of having one or more sons between the two study groups arranged according to digit ratio.

|          | No. of sons ≥ 1 | No. of sons = 0 | p-value | RR  | 95% CI   |
|----------|-----------------|-----------------|---------|-----|----------|
| Males    |                 |                 |         |     |          |
| DR < 0.95| 106             | 35              | 0.433   | 0.948| 0.830–1.082 |
| DR > 0.95| 92              | 24              |         |     |          |
| Females  |                 |                 |         |     |          |
| DR < 0.95| 107             | 14              | 0.024   | 1.138| 1.017–1.274 |
| DR > 0.95| 101             | 29              |         |     |          |

Relative risk (RR) analysis was used to compare variables of the two study groups arranged according to digit ratio. DR, digit ratio (2nd digit length / 4th digit length).

Table 6. Comparison of offspring sex ratio according to the number of total offspring.

|          | No. of total offspring | Number of sons | p-value | RR  | 95% CI   |
|----------|------------------------|----------------|---------|-----|----------|
| Males    |                        |                |         |     |          |
| N        | 114                    | 326            | 0.433   | 0.948| 0.830–1.082 |
| Offspring sex ratio | 0.667 ± 0.473*†         | 0.541 ± 0.327*† |       | 0.443 ± 0.269† |
| Females  |                        |                |         |     |          |
| N        | 63                     | 166            | 0.433   | 0.948| 0.830–1.082 |
| Offspring sex ratio | 0.667 ± 0.475*†         | 0.521 ± 0.345* |       | 0.452 ± 0.261† |
|          |                        |                |         |     |          |
| Total    |                        |                |         |     |          |
| N        | 174                    | 492            | 0.433   | 0.948| 0.830–1.082 |
| Offspring sex ratio | 0.667 ± 0.476†         | 0.563 ± 0.306    |       | 0.437 ± 0.277† |

p-value < 0.05 on one-way analysis of variance (ANOVA) with post hoc Bonferroni test.

*: between the patients with number of total offspring = 1 and the patients with number of total offspring = 2.
†: between the patients with number of total offspring = 1 and the patients with number of total offspring ≥ 3.
Recently, Ventura et al. [20] measured the digit ratio of 106 newborn infants and evaluated its relationship with the maternal digit ratio and maternal testosterone levels in plasma and amniotic fluid. Maternal plasma testosterone concentrations had a negative weak correlation with the digit ratio of both male and female newborns [20]. Mothers who gave birth to sons had lower digit ratios than those who had daughters [20]. These findings indicate that maternal hormone levels play important roles in determining the offspring's sex [20]. This means that the women presumed to have been exposed to higher levels of testosterone *in utero* gave birth to significantly more male offspring [12].

Meanwhile, Helle & Lilley showed that maternal digit ratio was not a predictor of lifetime offspring sex ratio [19]. One possible answer is that Helle’s sample is of indirectly measured digit ratio and the repeatability of digit ratio measurement is very low ($r = 0.79$). Furthermore, Helle’s sample has also been used to refute a link between offspring sex ratio and age at menarche when it is likely that such a link exists. Fukuda et al. reported that women who had an early age at menarche tended to have an excess of daughters [60]. This suggests that early menarche should be linked to high digit ratio. This has indeed been reported, first by Matchock [61] and then in two large samples by Manning and Fink [62] and Kalichman et al. [63]. However, Helle [64] using the same sample of 241 postmenopausal Finnish women having a total of 494 singleton offspring as before reported no link between digit ratio and age at menarche. It has been

**Table 7. Pearson’s linear correlation analysis of the patients with two or more children.**

| Offspring sex ratio | Males (N = 194) | r     | p-value |
|---------------------|----------------|-------|---------|
| Age                 | 0.058          | 0.418 |
| Height              | -0.100         | 0.167 |
| Weight              | -0.067         | 0.350 |
| Digit ratio         | 0.131          | 0.069 |

| Females (N = 200)  | r     | p-value |
|--------------------|-------|---------|
| Age                | -0.131| 0.065   |
| Height             | 0.039 | 0.583   |
| Weight             | 0.008 | 0.916   |
| Digit ratio        | -0.149| 0.035   |

Digit ratio, 2nd digit length / 4th digit length.

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**Table 8. Multiple linear regression analysis of the patients with two or more children.**

| Offspring sex ratio | B     | p-value |
|---------------------|-------|---------|
| Males (N = 194)     |       |         |
| Age                 | 0.002 | 0.530   |
| Height              | -0.004| 0.425   |
| Weight              | -0.001| 0.750   |
| Digit ratio         | 1.400 | 0.068   |

| Females (N = 200)   |       |         |
|---------------------|-------|---------|
| Age                 | -0.007| 0.073   |
| Height              | 0.001 | 0.896   |
| Weight              | 0.000 | 0.905   |
| Digit ratio         | -1.310| 0.029   |

Digit ratio, 2nd digit length / 4th digit length.

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suggested that Helle’s sample of Finnish women is small and atypical in at least some respects [65].

To date, the studies about the association between parental age and offspring sex ratio are controversial [66–68]. Our results showed that age was not related to digit ratio and offspring sex ratio (Table 2). However, in the present study, we did not investigate the patients’ age at the time of the birth. Actually, we investigated the patients’ age at the time of the investigation. Thus, we think that it is difficult to find the age effect on sex ratio in our data.

Birth data in Sweden for the period 1869–2004 showed that among live births the secondary sex ratio was on average 105.9 among singletons, 103.2 among twins and 99.1 among triplets [69]. This means that offspring sex ratio may be highest among singletons, medium among twins and lowest among triplets. However, in the present study, we investigated just the number of offspring. We did not distinguish multiples (twins and triplets) from singletons. In the present study, mean and median values of digit ratios of males, females, and all the patients are very close to 0.95. Therefore, we divided all the patients into two groups according to digit ratio cutoff of 0.95 (digit ratio < 0.95 versus digit ratio ≥ 0.95). Actually, when we divided the subjects according to median value of digit ratio in each sex, these results are similar to previous results with digit ratio cutoff of 0.95. Therefore, we think that digit ratio cutoff of 0.95 is appropriate. Additionally, in our previous studies, we also divided the subjects according to digit ratio cutoff of 0.95 [73–75].

Son preference and sex selective abortion have led to male-biased sex ratios in Asia, such as China, Korea, Vietnam, and India [76–87]. Even in this very low fertility society, such as Korea, son preference is a significant predictor of women’s practice of induced abortion [83]. Thus, these studies showed that induced abortion might be one of the evidences of artificial (man-made) sex selection. Therefore, it makes sense to exclude patients with a history of induced abortion that artificially affected the offspring sex ratio. However, spontaneous abortion, that is, intrauterine loss of fetuses might be one of the natural mechanisms that determine offspring sex ratio [88–92]. It has been suggested that stress exposure in early pregnancy can reduce male births via two mechanisms 1) reduced conception of males [93,94], and 2) increased intrauterine loss of male fetuses [89–92]. Therefore, we did not exclude patients with a history of spontaneous abortion.

**Limitations**

The current study had some limitations. The participants were just recruited from among patients who were hospitalized for urological surgery at a single tertiary academic center and may therefore not accurately represent the general population. Nevertheless, we believe that our study produced sufficient evidence of a relationship between maternal digit ratio and offspring sex ratio since we excluded patients with a history of induced abortion that artificially affected the offspring sex ratio.

Another limitation of this study was that serum testosterone levels were not measured. We performed the present investigation based on the assumption that digit ratio is indicative of...
steroid hormone activity among individuals. If this assumption is correct, we think that our findings may reflect the relationship between steroid hormone activity among individuals and offspring sex ratio.

Conclusions
In the present study, maternal (rather than paternal) digit ratio was negatively associated with offspring sex ratio. Females with a lower digit ratio were more likely to have more male offspring compared to those with a higher digit ratio. Overall, it could be suggested that the sex of offspring might be more influenced by maternal rather than paternal factors.

Ethical Standards
Ethical approval (approval number: GBIRB2013–88) was obtained from the Institutional Review Board (IRB) of Gachon University Gil Hospital (Incheon, Republic of Korea). Our study was conducted according to the ethical principles laid down in the 1964 Declaration of Helsinki and its later amendments.

Supporting Information
S1 Dataset. Raw data of all 508 patients. Sex: 1 = male, 2 = female; Ht, Height; Wt, Weight; BMI, Body mass index; DR, Digit ratio; S, number of sons; D, number of daughters; T, number of total offsprings; SR, offspring sex ratio.

Author Contributions
Conceived and designed the experiments: TBK SWK. Performed the experiments: TBK JKO. Analyzed the data: KTK SJY. Wrote the paper: TBK SWK.

References
1. Manning JT, Scutt D, Wilson J, Lewis-Jones Di (1998) The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentrations of testosterone, luteinizing hormone and oestrogen. Hum Reprod 13: 3000–3004. PMID: 9853845
2. Phelps VR (1952) Relative index finger length as a sex-influenced trait in man. Am J Hum Genet 4: 72–89. PMID: 14943709
3. Peters M, Mackenzie K, Bryden P (2002) Finger length and distal finger extent patterns in humans. Am J Phys Anthropol 117: 209–217. PMID: 11842400
4. Hönekopp J, Watson S (2010) Meta-Analysis of digit ratio 2D:4D shows greater sex difference in the right hand. Am J Hum Biol 22: 619–630. doi: 10.1002/ajhb.21054 PMID: 20737609
5. Lutchmaya S, Baron-Cohen S, Raggatt P, Knickmeyer R, Manning JT (2004) 2nd to 4th digit ratios, fetal testosterone and estradiol. Early Hum Dev 77: 23–28. PMID: 15113628
6. Malas MA, Dogan S, Evcil EH, Desdicioglu K (2006) Fetal development of the hand, digits and digit ratio (2D:4D). Early Hum Dev 82: 469–475. PMID: 16473482
7. Galis F, Ten Broek CM, Van Dongen S, Wijnaendts LC (2010) Sexual dimorphism in the prenatal digit ratio (2D:4D). Arch Sex Behav 39: 57–62. doi: 10.1007/s10508-009-9485-7 PMID: 19301112
8. Garn SM, Burdi AR, Babler WJ, Stinson S (1975) Early prenatal attainment of adult metacarpal-phalangeal rankings and proportions. Am J Phys Anthropol 43: 327–332. PMID: 1211429
9. Dean A, Sharpe RM (2013) Clinical review: Anogenital distance or digit length ratio as measures of fetal androgen exposure: relationship to male reproductive development and its disorders. J Clin Endocrinol Metab 98: 2230–2238. doi: 10.1210/jc.2012-4057 PMID: 23569219
10. Abbott AD, Colman RJ, Tiefenthaler R, Dumescic DA, Abbott DH (2012) Early-to-mid gestation fetal testosterone increases right hand 2D:4D finger length ratio in polycystic ovary syndrome-like monkeys. PLoS One 7: e42372. doi: 10.1371/journal.pone.0042372 PMID: 22927929
11. Berenbaum SA, Bryk KK, Nowak N, Quigley CA, Moffat S (2009) Fingers as a marker of prenatal androgen exposure. Endocrinology 150: 5119–5124. doi: 10.1210/en.2009-0774 PMID: 19819951
12. Grant VJ (2008) Sex-of-offspring differences between mothers. Evolutionary Psychology 6: 147–160.
13. Hollier LP, Keelan JA, Jamnadass ES, Maybery MT, Hickey M, Whitehouse AJ (2015) Adult digit ratio (2D:4D) is not related to umbilical cord androgen or estrogen concentrations, their ratios or net bioactivity. Early Hum Dev 91: 111–117. doi: 10.1016/j.earlhumdev.2014.12.011 PMID: 25594498
14. Manning JT (2002) Digit ratio: A pointer to fertility, behavior and health. New Brunswick, New Jersey: Rutgers University Press, p. 33.
15. Grant VJ (2007) Could maternal testosterone levels govern mammalian sex ratio deviations? J Theor Biol 246: 708–719. PMID: 17379251
16. James WH (2008) Evidence that mammalian sex ratios at birth are partially controlled by parental hormone levels around the time of conception. J Endocrinol 198: 3–15. doi: 10.1677/JOE-07-0446 PMID: 18577567
17. Perret M (2005) Relationship between urinary estrogen levels before conception and sex ratio at birth in a primate, the grey mouse lemur. Hum Reprod 20: 1504–1510. PMID: 15799612
18. Manning JT, Martin S, Trivers RL, Soler M (2002) 2nd to 4th digit ratio and offspring sex ratio. J Theor Biol 217: 93–95. PMID: 12183133
19. Helle S, Lilley T (2008) Maternal 2nd to 4th digit ratio does not predict lifetime offspring sex ratio at birth. Am J Hum Biol 20: 700–703. doi: 10.1002/ajhb.20796 PMID: 18561146
20. Ventura T, Gomes MC, Pita A, Neto MT, Taylor A (2013) Digit ratio (2D:4D) in newborns: influences of prenatal testosterone and maternal environment. Early Hum Dev 89: 107–112. doi: 10.1016/j.earlhumdev.2012.08.009 PMID: 23017880
21. Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1: 307–310. PMID: 2868172
22. Trivers RL, Willard D (1973) Natural selection of parental ability to vary the sex ratio of offspring. Science 179: 90–92. PMID: 4682135
23. Cameron EZ (2004) Facultative adjustment of mammalian sex ratios in support of the Trivers–Willard hypothesis: evidence for a mechanism. Proc Biol Sci 271: 1723–1728. PMID: 15306293
24. Grant VJ (1996) Sex determination and the maternal dominance hypothesis. Hum Reprod 11: 2371–2375. PMID: 8981113
25. Rosenfeld CS, Grimm KM, Livingston KA, Brokman AM, Lamberson WE, Roberts RM (2003) Striking variation in the sex ratio of pups born to mice according to whether maternal diet is high in fat or carbohydrate. Proc Natl Acad Sci U S A 100: 4628–4632. PMID: 12672968
26. Rosenfeld CS, Roberts RM (2004) Maternal diet and other factors affecting offspring sex ratio: a review. Biol Reprod 71: 1063–1070. PMID: 15229140
27. Cameron EZ, Lemons PR, Bateman PW, Bennett NC (2008) Experimental alteration of litter sex ratios in a mammal. Proc Biol Sci 275: 323–327. PMID: 18048284
28. Mathews F, Johnson PJ, Neil A (2008) You are what your mother eats: evidence for maternal preconception diet influencing foetal sex in humans. Proc Biol Sci 275: 1661–1668. doi: 10.1098/rspb.2008.0105 PMID: 18430648
29. Alexenko AP, Mao J, Ellersieck MR, Davis AM, Whyte JJ, Rosenfeld CS, et al. (2007) The contrasting effects of ad libitum and restricted feeding of a diet very high in saturated fats on sex ratio and metabolic hormones in mice. Biol Reprod 77: 599–604. PMID: 17522073
30. Fountain ED, Mao J, Whyte JJ, Mueller KE, Ellersieck MR, Will MJ, et al. (2008) Effects of diets enriched in omega-3 and omega-6 polyunsaturated fatty acids and offspring sex-ratio and maternal behaviour in mice. Biol Reprod 78: 211–217. PMID: 17928632
31. Green MP, Spate LD, Parks TE, Kimura K, Murphy CN, Williams JE, et al. (2008) Nutritional skewing of conceptus sex in sheep: effects of a maternal diet enriched in rumen-protected polyunsaturated fatty acids (PUFA). Reprod Biol Endocrinol 6: 21. doi: 10.1186/1477-7827-6-21 PMID: 18541015
32. Kimura K, Spate LD, Green MP, Roberts RM (2005) Effects of D-glucose concentration, D-fructose, and inhibitors of enzymes of the pentose phosphate pathway on the development and sex ratio of bovine blastocysts. Mol Reprod Dev 72: 201–207. PMID: 15968626
33. Grant VJ, Chamley LW (2010) Can mammalian mothers influence the sex of their offspring peri-conceptually? Reproduction 140: 425–433. doi: 10.1530/REP-10-0137 PMID: 20591970
34. Kimura K, IWata H, Thompson JG (2008) The effect of glucosamine concentration on the development and sex ratio of bovine embryos. Anim Reprod Sci 103: 228–238. PMID: 17198747
35. Mittwoch U (1989) Sex differentiation in mammals and tempo of growth: probabilities vs. switches. J Theor Biol 137: 445–455. PMID: 2626060
36. Mittwoch U (1996) Differential implantation rates and variations in the sex ratio. Hum Reprod 11: 8–9. PMID: 8671148
37. Ray PF, Conaghan J, Winston RM, Handside AH (1995) Increased number of cells and metabolic activity in male human preimplantation embryos following in vitro fertilization. J Reprod Fertil 104: 165–171. PMID: 7636798
38. Permagent E, Fiddler M, Cho N, Johnson D, Holmgren WJ (1994) Sexual differentiation and preimplantation cell growth. Hum Reprod 9: 273–280. PMID: 7475115
39. Gibson MA, Mace R (2003) Strong mothers bear more sons in rural Ethiopia. Proc Biol Sci 270 Suppl 1: S108–S109. PMID: 12952651
40. Andersson R, Bergstrom S (1998) Is maternal malnutrition associated with a low sex ratio at birth? Hum Biol 70:1101–1106. PMID: 9825599
41. Cagnacci A, Renzi A, Arangino S, Alessandrinii C, Volpe A (2004) Influences of maternal weight on the secondary sex ratio of offspring. Hum Reprod 19: 442–444. PMID: 14747194
42. Wells JC (2000) Natural selection and sex differences in morbidity and mortality in early life. J Theor Biol 7: 65–76.
43. Tamimi RM, Lagiou P, Mucci LA, Hsieh CC, Adami HO, Trichopoulos D (2003) Average energy intake among pregnant women carrying a boy compared with a girl. Brit Med J 328: 1245–1246. PMID: 12791740
44. Cameron EZ, Linklater WL (2007) Extreme sex ratio variation in relation to change in condition around conception. Biol Lett 3: 395–397. PMID: 17439844
45. Graffelman J, Hoekstra RF (2000) A statistical analysis of the effect of warfare on the human secondary sex ratio. Hum Biol 72: 433–445. PMID: 10885189
46. MacMahon B, Pugh TF (1954) Sex ratio of white births in the United States during the Second World War. Am J Hum Genet 6: 284–292. PMID: 13158334
47. Clutton-Brock TH, Albon SD, Guinness FE (1984) Maternal dominance, breeding success and birth sex ratios in red deer. Nature 308: 358–360.
48. Sheldon BC, West SA (2004) Maternal dominance, maternal condition, and offspring sex ratio in ungulate mammals. Am Nat 163: 40–54. PMID: 14767835
49. Grant VJ (1994) Maternal dominance and the conception of sons. Br J Med Psychol 67: 343–351. PMID: 7888397
50. Bouissou MF (1978) Effects of testosterone propionate on dominance relationships in cows. Horm Behav 11: 388–400. PMID: 753701
51. Christiansen K. Behavioural correlates of testosterone. In: Nieschlag E, Behre HMeditors. Testoster- one: action, deficiency, substitution. New York: Springer Verlag; 1998. pp. 107–142.
52. Grant VJ, France JT (2001) Dominance and testosterone in women. Biol Psychol 58: 41–47. PMID: 11473794
53. Shargal D, Shore L, Roteri N, Terkel A, Zorovsky Y, Shemesh M, et al. (2008) Fecal testosterone is elevated in high ranking female ibexes (Capra nubiana) and associated with increased aggression and a preponderance of male offspring. Theriogenology 69: 673–680. doi: 10.1016/j.theriogenology.2007.11.017 PMID: 18242693
54. Heille S, Laaksonen T, Adamsson A, Paranko J, Hulttus O (2008) Female field voles with high testosterone and glucose levels produce male-biased litters. Animal Behaviour 75: 1031–1039.
55. Grant VJ, Irwin RJ (2005) Follicular fluid steroid levels and subsequent sex of bovine embryos. J Exp Zool A Comp Exp Biol 303: 1120–1125. PMID: 16254922
56. Grant VJ, Irwin RJ, Standley NT, Shelling AN, Chamley LW (2008) Sex of bovine embryos may be related to mothers’ preovulatory follicular testosterone. Biol Reprod 78: 812–815. doi: 10.1095/ biolreprod.107.066050 PMID: 18184920
57. Garcia-Herreros M, Bermejo-Alvarez P, Rizos D, Gutierrez-Adan A, Fahey AG, Lonergan P (2010) Intrafollicular testosterone concentration and sex ratio in individually cultured bovine embryos. Reprod Ferti Dev 22: 533–538. doi: 10.1071/RD09157 PMID: 20188026
58. Fukuda M, Fukuda K, Shimizu T, Nobunaga M, Grete Byskov A, Yding Andersen C (2011) The sex ratio of offspring is associated with the mothers’ age at menarche. Hum Reprod 26: 1551–1554. doi: 10.1093/humrep/der107 PMID: 21467205
61. Matchock RL (2008) Low digit ratio (2D:4D) is associated with delayed menarche. Am J Hum Biol 20: 487–489. doi: 10.1002/ajhb.20763 PMID: 18348172

62. Manning JT, Fink B (2011) Is low digit ratio linked with late menarche? Evidence from the BBC internet study. Am J Hum Biol 23: 527–533. doi: 10.1002/ajhb.21186 PMID: 21547980

63. Kalichman L, Batsevich V, Kobyliansky E (2013) 2D:4D finger length ratio and reproductive indices in a Chuvashian population. Am J Hum Biol 25: 617–621. doi: 10.1002/ajhb.22420 PMID: 23907730

64. Helle S (2011) Women’s age at menarche and offspring sex ratio. Hum Reprod 26: 2588–2589. doi: 10.1093/humrep/der204 PMID: 21685137

65. Fukuda M, Fukuda K, Shimizu T, Nobunaga M, Grete Byskov A, Yding Andersen C (2011) Reply: The sex ratio of offspring is associated with the mother’s age at menarche. Hum Reprod 26: 2589–2590.

66. Matsu K, Ushioda N, Udoff LC (2009) Parental aging synergistically decreases offspring sex ratio. J Obstet Gynaecol Res 35: 164–168. doi: 10.1111/j.1447-0756.2008.00836.x PMID: 19215965

67. Ein-Mor E, Mankuta D, Hochner-Celnikier D, Hurwitz A, Haimov-Kochman R (2010) Sex ratio is remarkably constant. Fertil Steril 93: 1961–1965. doi: 10.1016/j.fertnstert.2008.12.036 PMID: 19159875

68. Williams TJ, Pepitone ME, Christensen SE, Cooke BM, Huberman AD, Breedlove NJ, et al. (2000) Finger-length ratios and sexual orientation. Nature 404: 455–456. PMID: 10761903

69. Coates JM, Gurnell M, Rustichini A (2009) Second-to-fourth digit ratio predicts success among high-frequency financial traders. Proc Natl Acad Sci USA 106: 623–628. doi: 10.1073/pnas.0810907106 PMID: 19139402

70. Manning JT, Churchill AJ, Peters M (2007) The effects of sex, ethnicity, and sexual orientation on self-measured digit ratio (2D:4D). Arch Sex Behav 36: 223–233. PMID: 17373585

71. Jung H, Kim KH, Yoon SJ, Kim TB (2011) Second to fourth digit ratio: a predictor of prostate-specific antigen level and the presence of prostate cancer. BJU Int 107: 591–596. doi: 10.1111/j.1445-410X.2010.09490.x PMID: 20633006

72. Kim TB, Oh JK, Kim KH, Jung H, Yoon SJ, Lee MS, et al. (2012) Dutasteride, who is more effective for Second to fourth digit ratio and the relationship with prostate volume reduction by dutasteride treatment. BJU Int 110(11 Pt C): E857–E863. doi: 10.1111/j.1445-410X.2012.11343.x PMID: 22755506

73. Oh JK, Kim KH, Jung H, Yoon SJ, Kim TB (2012) Second to fourth digit ratio: its relationship with core cancer volume and Gleason score in prostate biopsy. Int Braz J Urol 38: 611–619. PMID: 23131519

74. Almond D, Edlund L (2008) Son-biased sex ratios in the 2000 United States Census. Proc Natl Acad Sci U S A 105: 5681–5682. doi: 10.1073/pnas.0800703105 PMID: 18378890

75. Chun H, Kim IH, Khang YH (2009) Trends in sex ratio at birth according to parental social positions: results from vital statistics birth, 1981–2004 in Korea. J Prev Med Public Health 42: 143–150. doi: 10.3961/jpmph.2009.42.2.143 PMID: 19349745

76. Westly SB, Choe Kim M (2007) How does son preference affect population in Asia? Asia Pacific Issues 84: 1–12.

77. Miller BD (2001) Female-selective abortion in Asia: Patterns, policies, and debates. Am Anthropol 103: 1083–1095. PMID: 12769123

78. Kim DS (2004) Missing girls in South Korea: Trends, levels and regional variations. Population 59: 865–878.

79. Chung W, Das Gupta M (2007) The decline of son preference in South Korea: The roles of development and public policy. Popul Dev Rev 33: 757–783.

80. Park CB, Cho NH (1995) Consequences of son preferences in a low-fertility society: Imbalance of the sex ratio at birth in Korea. Popula Rev 21: 78–84.

81. Chung W (2007) The relation of son preference and religion to induced abortion: the case of South Korea. J Biosoc Sci 39: 707–719. PMID: 17381891

82. Hesketh T (2011) Selecting sex: the effect of preferring sons. Early Hum Dev 87: 759–761. doi: 10.1016/j.earlhumdev.2011.08.016 PMID: 21920680

83. Zhou C, Wang XL, Zhou XD, Hesketh T (2012) Son preference and sex-selective abortion in China: informing policy options. Int J Public Health 57: 459–465. doi: 10.1007/s00038-011-0267-3 PMID: 21681450

84. Bélanger D, Oanh KT (2009) Second-trimester abortions and sex-selection of children in Hanoi, Vietnam. Popul Stud (Camb) 63: 163–171.
87. Nidadavolu V, Bracken H (2006) Abortion and sex determination: conflicting messages in information materials in a District of Rajasthan, India. Reprod Health Matters 14: 160–171. PMID: 16713891

88. Grant VJ, Irwin RJ (2009) A simple model for adaptive variation in the sex ratios of mammalian offspring. J Theor Biol 258: 38–42. doi: 10.1016/j.jtbi.2009.01.013 PMID: 19490877

89. Catalano R, Ahern J, Bruckner T, Anderson E, Saxton K (2009) Gender-specific selection in utero among contemporary human birth cohorts. Paediatr Perinat Epidemiol 23: 273–278. doi: 10.1111/j.1365-3016.2009.01028.x PMID: 19775389

90. Catalano RA, Saxton K, Bruckner T, Goldman S, Anderson E (2009) A sex-specific test of selection in utero. J Theor Biol 257: 475–479. doi: 10.1016/j.jtbi.2008.12.008 PMID: 19146859

91. Catalano R, Yorifuji T, Kawachi I (2013) Natural selection in utero: evidence from the Great East Japan Earthquake. Am J Hum Biol 25: 555–559. doi: 10.1002/ajhb.22414 PMID: 23754635

92. Catalano RA, Saxton KB, Bruckner TA, Pearl M, Anderson E, Goldman-Mellor S, Margerison-Zilko C, Subbaraman M, Currier RJ, Kharrazi M (2012) Hormonal evidence supports the theory of selection in utero. Am J Hum Biol 24: 526–532. doi: 10.1002/ajhb.22265 PMID: 22411168

93. Fukuda M, Fukuda K, Shimizu T, Meller H (1998) Decline in sex ratio at birth after Kobe earthquake. Hum Reprod 13: 2321–2322. PMID: 9756319

94. Torche F, Kleinhaus K (2012) Prenatal stress, gestational age and secondary sex ratio: the sex-specific effects of exposure to a natural disaster in early pregnancy. Hum Reprod 27: 568–567. doi: 10.1093/humrep/der390 PMID: 22157912