



ORIGINAL ARTICLE

A preliminary analysis of the secondary sex ratio decline after the COVID-19 pandemic in Japan

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Abstract

Objectives: The secondary sex ratio (SSR, i.e., the number of male births per 100 female births) has long been proposed as a sentinel health indicator. Studies have suggested that exogenous environmental stressors reduce SSR after 3 to 6 months (via disproportionate male fetus deaths) and after 9 months (via reduced male conception). We aimed to examine whether SSR declined after the coronavirus disease 2019 (COVID-19) pandemic in Japan.

Methods: We used monthly vital statistics records collected between January 2013 and April 2021 (the -number of male and female live births, in particular). Using information reported before the pandemic struck Japan (i.e., January 2013 to January 2020), we predicted SSRs for the months after the pandemic (i.e., February 2020 to April 2021) and compared reported and predicted SSRs. We also stratified the analysis by including two groups of prefectures with different degrees of possible influence from the pandemic.

Results: We observed a significant reduction in SSR during December 2020 of 102.81 (i.e., 9–10 months after the pandemic affected the country), which was below the lower bound of the 95% prediction intervals (103.12–106.33). This was the lowest SSR observed during the 100-month study period. In addition, the reduction in SSR during December 2020 was more pronounced in the more seriously affected prefectures.

Conclusion: In Japan, we found a significant reduction in SSR (i.e., fewer male live births) 9–10 months after COVID-19 was declared a pandemic. This suggests the onset of the COVID-19 pandemic was a significant population-level stressor.

1 | INTRODUCTION

The secondary sex ratio (SSR), that is, the number of male births per 100 female births, is a sentinel health indicator that reflects population health and informs policy decisions in healthcare (Allan et al., 1997; Davis et al., 1998; Davis et al., 2007). Studies have reported reductions in SSR (i.e., fewer male births) associated with several population-level stressors, such as terrorist attacks (Bruckner et al., 2019; Grech, 2015; Masukume

et al., 2017), wars (Ansari-Lari & Saadat, 2002; Zorn et al., 2002), and earthquakes (Catalano et al., 2013; Fukuda et al., 1998; Fukuda et al., 2018; Hamamatsu et al., 2014) albeit with several exceptions (Grech & Scherb, 2015; Khashan et al., 2009; Kolk & Schnettler, 2016; Schnettler & Klüsener, 2014). It was hypothesized that population-level stressors induce natural selection against males (via disproportionate fetal deaths and reduced conception in males vs. females).

In the literature, the time taken for the effect of environmental stressors on SSR to appear varied from as early as 1 month (Bruckner et al., 2019) to 9–10 months after exposure (i.e., the full gestation period) (e.g., Catalano et al., 2013). Bruckner and Catalano (2018) hypothesized that SSR reduces 3 months after exposure, which was interpreted as a result of disproportionate fetal deaths among males in the cohort exposed to the stressor at the 24th week of gestation (i.e., the last week in the critical period, which is the 16th–24th week of gestation) and born in the 36th week (i.e., the number of weeks of gestation for babies born relatively early). The effect was postulated to last until 24 weeks (6 months) after the exposure (i.e., the cohort exposed in the 16th week of gestation and was born in the 40th week). Research has also hypothesized that if stressors reduce male conception, SSR reduces 36–40 weeks after the shock (Catalano et al., 2013).

This study was designed to extend previous research by examining if the coronavirus disease (COVID-19), a respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that can cause multi-system involvement (e.g., brain, hematological system, liver, kidneys, and endocrine system) (Rana et al., 2021), was linked with a reduced SSR in Japan. The first COVID-19-related death was reported in February 2020; the Japanese government requested the closure of all schools from March 2, 2020, and later declared a state of emergency on April 7, 2020, in seven prefectures. This state of emergency was expanded to the whole country from April 16 until May 25, 2020. In the meantime, the World Health Organization (WHO) declared the COVID-19 outbreak a global pandemic on March 11, 2020. While the number of COVID-19-related deaths in Japan has remained lower than those reported in more severely affected countries (WHO, n.d.), it is possible that restrictions in social and economic activities as exemplified by a decline in mobility in the early phase of the pandemic (Nagata et al., 2021) or fear of the virus which could have been worsened by the frequent media exposure to COVID-19-related information (Liu et al., 2020; Ng et al., 2021) affected SSR via increased psychosocial stress imposed on expectant mothers. This supposition has been previously hypothesized by Abdoli (2020). It should be noted that this situation differed from those examined in previous studies in that the population had been long exposed to the stressor for a certain period of time.

Thus, this study aimed to examine whether the COVID-19 pandemic was linked with a decline in SSR among the Japanese population, using the number of births reported in the Vital Statistics Records of Japan. Based on the literature, we hypothesized that SSR starts to reduce after exposure to the stressor and the effects

continue to express themselves in terms of disproportionate male fetal deaths (when compared to female fetal deaths) and reduced conception in male versus female fetuses. We also stratified the analysis into two groups of prefectures which experienced different degrees of severity with regard to COVID-19, assuming that we would observe a larger reduction in SSR in the more affected prefectures, compared with the less affected ones.

2 | MATERIALS AND METHODS

We used publicly available monthly prefecture-level vital statistics records in Japan (the number of male and female live births, in particular) that were collected during the period between January 2013 and April 2021 (100 months) (Ministry of Health, Labour and Welfare, n.d.). Virtually all the births were deemed officially registered in Japan (Cappa & Wardlaw, 2013). As Japan experienced the Great East Japan Earthquake in March 2011, which has been studied in relation to SSR (Catalano et al., 2013; Hamamatsu et al., 2014), we decided not to include records that could have been influenced by that catastrophe. In addition, the number of births registered outside of Japan or unknown locations were not included in subsequent analyses. According to Japan's Ethics Guideline for Epidemiological Research, ethical clearance, and informed consent were not required as this study does not involve individual-level data.

We predicted SSRs for the months after the COVID-19 pandemic (i.e., February 2020–April 2021) using information reported for the period before the pandemic (i.e., January 2013–January 2020). More specifically, after testing stationarity with the Dickey–Fuller test ($p < .001$), we used an autoregressive moving average (ARMA) model with minimum Akaike Information Criterion (AIC) (i.e., AR [3] and MA [2]) to fit SSRs for January 2013–January 2020 (Table S1). The estimates obtained in this model were used to predict the SSR for the months after the pandemic outbreak. We used the “predict” command in Stata with the “mse” option to calculate the 95% upper and lower bounds of the predicted SSRs in given months (i.e., prediction intervals [PI]) (StataCorp, 2019).

We also conducted stratified analyses by considering two groups of prefectures with different degrees of possible influence from COVID-19: (1) 13 prefectures that were designated as the “special alert” prefectures by the government (*Tokutei Keikai Todofuken*; that is, Hokkaido, Tokyo, Kanagawa, Chiba, Saitama, Osaka, Hyogo, Kyoto, Ibaraki, Aichi, Gifu, Ishikawa, and Fukuoka) and (2) the remaining prefectures ($n = 34$). The determination of the 13 prefectures as special alert prefectures by the government was based on a variety of information

including the cumulative number of cases (>100 cases), the proportion of cases infected by an unknown source ($\geq 50\%$), and short doubling time (<10 days) (Ministry of Health, Labour and Welfare, 2020). Those living in the more severely affected prefecture were strongly requested to refrain from going out; events were canceled, and venues and facilities were closed. The same parameters (i.e., AR [3] and MA [2]) were used for the analyses in the more and less affected prefectures.

Statistical analyses were conducted using Stata ver. 16.0 (Stata Corp., College Station, TX).

3 | RESULTS

A total of 7 835 985 live births (4 017 899 male live births and 3 818 086 female live births) were registered between January 2013 and April 2021. Figure 1 shows reported SSRs for the entire country (green), the more heavily affected prefectures (blue), and the less affected prefectures (orange). The highest and lowest SSRs for the entire country during the study period were 107.83 (July 2016) and 102.81 (December 2020), respectively.

Figure 2 shows the observed and predicted SSR based on the ARMA model. We found a statistically significant reduction in SSR in December 2020 (102.81), which was lower than the lower bound of 95% PI (i.e., 103.12). Detailed information regarding the predicted SSR and corresponding PIs are also shown in Table S2.

When the analyses were stratified by prefectures with different levels of possible influence from COVID-19, the SSR reduced in December 2020 only among the more severely affected prefectures (Figures S1 and S2, and Table S2). While we did not observe a significant reduction in SSR in the less affected prefectures, the observed

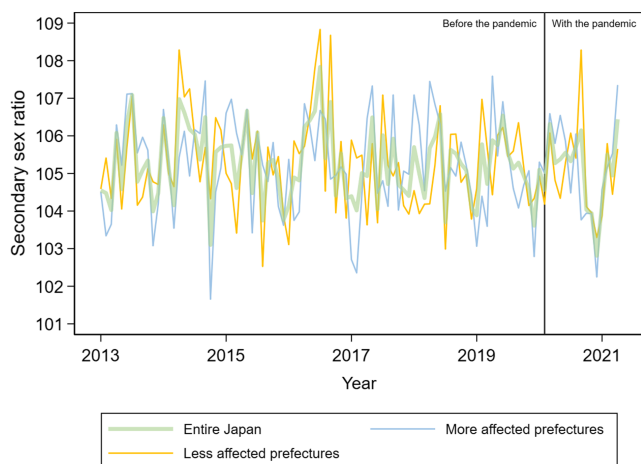


FIGURE 1 The transitions in monthly secondary sex ratio in Japan (January 2013–April 2021)

SSR was higher than the upper bound of prediction interval in September 2020.

4 | DISCUSSION

We examined whether SSR declined after the COVID-19 pandemic hit Japan and found a significant decline in SSR in December 2020, which is 9–10 months after the pandemic started to affect the country. This reduction in SSR was observed in the more severely affected prefectures. In the less affected prefectures, we did not find strong evidence of a significant reduction in SSR, but observed a significant increase in SSR in September 2020.

Our findings as regards the reduction in SSR observed in December 2020 agreed with the hypothesis that exogenous stressors induce lower male conception and thus lower SSR after 9 months and are in line with the previous literature that examined the associations in relation to terrorist attacks, wars, or an earthquake (Ansari-Lari & Saadat, 2002; Catalano et al., 2013; Fukuda et al., 1998; Fukuda et al., 2018; Grech, 2015; Hamamatsu et al., 2014; Masukume et al., 2017; Zorn et al., 2002). For example, Fukuda et al. (1998) reported a significant decline in the SSR in Hyogo Prefecture in October 1995, which was 9 months after the Kobe earthquake; the male proportion among newborn infants was 0.501 (equivalent to 1.004 under the SSR definition used in this study), which was lower than expected SSR of 0.516 (equivalent to 1.066 in this study).

While the COVID-19 pandemic (at least that which was experienced by Japanese people) was not as directly

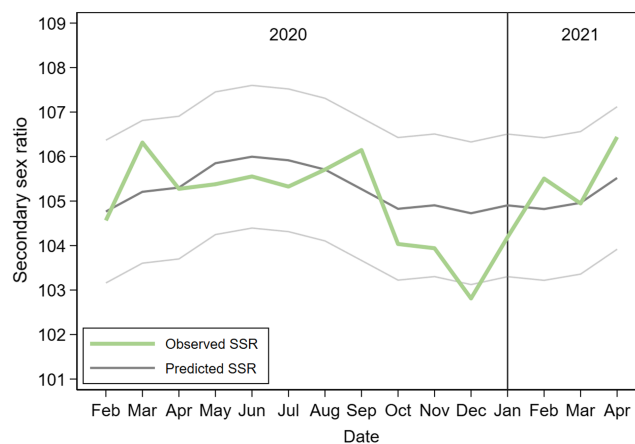


FIGURE 2 Observed and predicted secondary sex ratios after the COVID-19 pandemic in Japan (February 2020–April 2021). The light gray lines in the figure indicate the 95% upper and lower bounds of the predicted secondary sex ratios for a given month. Secondary sex ratios were predicted based on the secondary sex ratios reported between January 2013 and January 2020 ($n = 85$)



life-threatening as the abovementioned population-level stressors, our findings suggest that social and economic restrictions or fear of the virus associated with the pandemic can be strong enough to manifest itself as a decline in SSR. It is possible that people became increasingly anxious about their future when they faced the changes and uncertainty caused by the pandemic. This supposition is supported by a web-based survey conducted in March 2020 across the world reporting that biggest concerns of participants to be: health of friends, grandparents or loved ones (46.2%); healthcare collapse (19.5%); consequences of economy (18.1%); mass panic (15.3%); personal health (11.0%); societal breakdown (10.3%); and personal economy (9.6%) (Mertens et al., 2020). In addition, we should also account for the influence of the media. Ng et al. (2021) that studied news media narratives of COVID-19 across 20 countries documented that COVID-19-related topics rapidly dominated the global news narratives, reaching its peak in March 2020. While Japan was not included in their study, Japanese people were also likely to be frequently exposed to COVID-19-related information during the same time; December 2020 when we observed a significant SSR reduction is exactly 9 months after the “peak exposure.”

It should also be noted that our hypothesis regarding the effect of COVID-19 pandemic lasting longer than those examined in the previous studies was rejected, given that a reduction in SSR observed in December 2020 did not continue in the following months (Catalano et al., 2013; Hamamatsu et al., 2014). One possible interpretation of this is that people became adapted to the lifestyle changes after spending a relatively short period of time living through a pandemic; thus, no subsequent reduction in SSR was observed. Notably the null findings observed in January–April 2021 do not rule out the possibility of a reduction in SSR in the near future. COVID-19 has had an immense effect on the social and economic conditions of people. Sakamoto et al. (2021) studied suicide rates in Japan during the COVID-19 pandemic by comparing it to the preceding years and reported that suicide rates increased several months into the pandemic (October and November 2020 for males and from July through November 2020 for women). Given that the effects of exogenous environmental stressors on SSR do not become apparent until several months after the event, there may be another significant reduction in SSR in the future.

The SSR increased in the less severely affected prefectures in September 2020. We did not expect SSR to increase as a response to the pandemic and it could have been a chance finding. However, it should be mentioned that the Men's Rugby World Cup was hosted in Japan

from September to November 2019 although it was not the event that was experienced only by the less affected prefectures. This was the first time the Rugby World Cup was held in Asia and 13 000 volunteers participated in the event. The economic impact was estimated to be as much as 646.4 billion yen (equivalent to approximately 6 billion US dollars), which was the highest ever in the Rugby World Cup history (Oshimi et al., 2021; The Rugby World Cup 2019 Organizing Committee, 2020). Ten months after the end of the World Cup falls in September 2020 when we observed a significant increase in SSR. Interestingly, this increase in SSR was in line with a previous study that reported an increase in SSR 9 months after the 2010 FIFA World Cup in South Africa (Masukume & Grech, 2015) whereas the same authors reported a null finding after the 1998 FIFA World Cup in France (Masukume & Grech, 2016).

This study had several limitations. First, we did not have information on the sex ratio of aborted fetuses in the current data set. Thus, we could not directly test the hypothesis that COVID-19 induces disproportionate fetal deaths in males vs. females a few months into the pandemic. In addition, we could not examine if the pandemic affected SSR differentially via intrauterine mortality vs. reduced male conception. Second, a birth certificate is submitted to the municipality offices of either birthplace, residence, or legal domicile. It is possible that the place of birth registry used in our sensitivity analyses were different from the locations where they were (or were not) influenced by COVID-19; however, such a difference would have little effect on the observed association.

Future research should focus on how the subsequent surges of COVID-19 in Japan impacted SSR by using data collected for a longer period of time. It is possible that the development of COVID-19 vaccines might have helped people ease stress and feeling of anxiety (and thus, with no reduction in SSR observed) while at the same time, a worsening of personal economic situation might have put some people at higher risk of psychosocial stress leading to lower SSR. If we extend the study period to the post-COVID period, the analysis will also help us re-evaluate the changes in SSR observed in our current study by comparing the range of fluctuations in SSR before, during, and after the pandemic. It is also important to study the effect of COVID-19 pandemic on other demographic indicators to facilitate our understanding of human adaptation to the world with COVID-19. The effect of the COVID-19 pandemic on demographic indicators has also been reported by Catalano et al. (2021) whose study shows fewer male twins in birth cohorts exposed in utero to the onset of the COVID-19 pandemic in Norway.

5 | CONCLUSION

Using monthly vital statistics records in Japan, we found a significant reduction in SSR in December 2020, which was 9–10 months after the COVID-19 pandemic hit the country. This reduction in SSR was more pronounced in the more severely affected prefectures.

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CONFLICT OF INTEREST

The authors had no conflict of interest to declare.

AUTHOR CONTRIBUTIONS

Conceptualization: Yosuke Inoue, Tetsuya Mizoue. Formal analysis: Yosuke Inoue. Methodology: Yosuke Inoue. Writing – original draft: Yosuke Inoue. Writing – review & editing: Yosuke Inoue, Tetsuya Mizoue.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in Ministry of Health, Labour and Welfare, Japan at <https://www.mhlw.go.jp/toukei/list/81-1a.html>.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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