



Best practice guidelines

Seasonal inconstancy of human sex ratio at birth



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ABSTRACT

A large body of literature describes relationships between the sex ratio at birth and modifying factors. The relationships that display seasonal fluctuations are hypothesized to reflect causal impact of periconceptual and later intrauterine effects. This short review summarizes the results of studies that investigated internal and external influences on the seasonal pattern of human sex ratio at birth.

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1. Introduction

Sex ratio at birth (SRB) is known to vary according to region [1] and population [2], being dependent on environmental stress [3–5], ambient temperature and its monthly variation [6], nutritional status and caloric availability [7], socio-economic [8,9] and behavioural factors [10]. It has been reported that SRB may exhibit seasonal variation. A seasonal pattern has been documented for European countries [11–13], North America [14–17], Brazil [18] and Australia [19]. However, no uniform annual rhythm has been established. For larger countries, a unimodal pattern with a lower SRB in February and March and a higher

ratio in June and July has been observed [1]. The patterns of sex ratio fluctuation during the second half of the year had an indefinite character and varied from region to region. The curves based on smaller populations display a great deal of irregularity and a multimodal pattern with 3–4 peaks, which suggests that other conditions as well as seasons are relevant and influence SRB.

Furthermore, the seasonality of SRB is not a general phenomenon that applies universally to different regions and populations. Thus, while the marked seasonal pattern has been described for Japan [1], India [20], northeast China [21], Iran [22], it is relatively less in Germany [12], and absent in Malta [23], southwestern Finland [24], Scotland [25], Costa Rica [26], and Hausa, Africa [27]. After reviewing the monthly variation of SRB, James [16] concluded that there was evidence of seasonality for the United States only.

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Very recently, Orzack et al., having analysed a large dataset, reported a fundamental and somewhat revolutionary insight into early human development [28]. The authors' estimate of the sex ratio at conception is 0.5 contradicting the common claim that the primary ratio is male-biased. They state that there is male preponderance only among abnormal embryos, while in normal embryos, the ratio is female-biased. This unusual view needs support by other investigations.

2. Seasonal preovulatory overripeness ovopathy (SPrOO)

The SPrOO hypothesis contends that the modulation of the sex ratio at conception (and thus SRB) is seasonally dependent on ovopathy due to ova overripeness and the inherent preferential fertilization of nonoptimally matured oocytes by Y-bearing spermatoocytes [29]. While it is almost impossible to test this hypothesis, many facts have been accumulated in favour of this hypothesis, since this provides an explanation for many experimental findings and data in the field of human pathology [30].

3. Hormones

Preconceptional stress levels have been postulated to influence embryonic sex. Women with high salivary cortisol concentrations tend to more frequently give birth to male infants than their counterparts with lower cortisol levels. The authors of the study found it possible to relate cortisol level with the degree of stress [31].

James summarized the evidence that offspring sex ratios are causally related to the environment (and hence seasonality) via the hormone levels of both parents around the time of conception [32]. Thus, high levels of gonadotropins were suggested to predispose to the production of female zygotes whereas high paternal testosterone concentration favours males. Furthermore, increased maternal oestrogens are associated with sons and progesterones with daughters.

4. Mother's body weight

When the sex of at-term delivered fetuses was stratified for month of conception and for pregravid maternal weight, the seasonal pattern of SRB in Modena, Italy, was found to depend upon maternal weight: two peaks were observed if pregnancies were begun in March and October in mothers in the lowest two quartiles of initial weight, and one single maximum was observed if pregnancies were initiated in October in women with preconceptional weight in the upper two quartiles [33]. No annual rhythm could be established in secondary SRs stratified by month of birth [34]. The association between mother's body weight and sex ratio becomes understandable in view of the data on relations of fat tissue and sex steroids in a female organism [35,36].

5. External factors driving the annual rhythm of SRB

5.1. Socio-economic

In academic mothers at the University of Vienna but not in non-academic counterparts, the SRB increased during springtime and decreased in summer; thus displaying an annual rhythm [37]. Multiple logistic regression analyses revealed no significant effects of birth order and mother's age at childbirth. The authors concluded that the likely cause of this seasonal phenomenon is an interaction between socio-economic and environmental working conditions.

5.2. Temperature

In humans, studies regarding the association between ambient temperature and SRB have produced mixed results. A retrospective analysis of birth data for the Sami population from northern Finland in

the eighteenth and nineteenth centuries yielded an increased prevalence of male births in warmer years, as well as the converse [38].

However, no such findings were evident in New Zealand when relating ambient temperatures to the proportion of male births and stillbirths [39]. The absence of such effects may be related to regions with warmer climates and minor temperature variation across seasons.

A computerised literature search has not revealed publications related to this topic in regions with a climate as severe as that of Siberia. In order to evaluate temperature effects upon SRB, an analysis of bimonthly birth data from 1959 to 2001 was performed in Novosibirsk region, southwestern Siberia, for 1,296,371 live singleton births. The region has a continental climate with a pronounced difference of 38 °C in mean monthly temperatures between January and July and about 20 °C between March and May. Periodic regression analysis revealed significant annual rhythms of SRB in urban populations with an amplitude of 2.5% of the overall mean and a peak in late May [40]. Quarterly analysis yielded an amplitude of 1.2% [41]. No significant overall annual rhythm could be identified in rural populations because of bad synchronization between individual yearly rhythms; although they were well pronounced with the amplitudes ranging from 8.0% to 12.2%.

A comparison of these results showed more pronounced seasonal variation of SRB in Siberian inhabitants than in other populations. The minuscule monthly variation in the USA has even led James to the conclusion that seasonal factors can provide no useful clue to the causes of variation in sex ratio [42]. Nevertheless, the annual amplitude has been reported as being less than 1 percent for the United States [16] and Germany [12,43], about 1.3% for The Netherlands [11], 2.1% for Australia [19], and 2.5% for Novosibirsk region. Only the amplitudes for Quebec (7.6%) [17] and Japan (9.5%) [1] approach this value; although these were observed in the 17th and 18th centuries for the former and around the 1900s for the latter.

This suggests that the difference in the amplitudes observed is due to the severity of climate and mainly to the seasonal variation of air temperature. The reasons for this suggestion are based on the data on the involvement of ambient temperature in the control of sex ratio, obtained from population-based, observational and experimental studies [6,44,45]. Although environmental temperature has become physiologically less important over the last five decades due to the availability of central heating in urban populations, rural populations, at least in Siberia, are exposed to low temperatures in winter since they spend a significant amount of time outdoors because of the working conditions.

Male fetuses are more vulnerable than female fetuses and are eliminated more frequently in unfavourable conditions. Therefore, male foetuses born during stressful times, i.e. at the trough of annual SRB rhythm, may exhibit better health than those in other cohorts because fetal loss has already "culled" the frailest male organisms. On the contrary, at the peak of the rhythm, the probability of appearance of weak boys is greater. This hypothesis can be tested in prospective health studies. The finding of Catalano et al. supports this suggestion. Their study showed that cold ambient temperatures during pregnancy predict low SRB and longer life span of adult men in annual birth cohorts composed of Danes, Finns, Norwegians and Swedes born between 1878 and 1914 [46].

5.3. Precipitations

In equatorial countries with constant temperatures throughout the year, precipitation becomes the leading factor that drives the sex ratio. The rainy season relates to more male births in near-equatorial Nigeria [47] while just the opposite was found in Benin City [48]. It seems likely that it is not rain itself that influences SRB but other factor(s) associated with the rainy or dry season.

5.4. Poisons

Many studies have examined whether everyday toxins and occupational poisons affect SRB. Meta-analysis showed that paternal exposures

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