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Biological, Environmental, and Behavioural Determinants of Human Secondary Sex Ratio: A Systematic Literature Review and Critical Medical Analysis

Pardomuan Robinson Sihombing
robinson@bps.go.id
[1]BPS-Statictics Indonesia, Jl dr Sutomo no 6-8 Jakarta

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ABSTRACT

Introduction: This study presents a Systematic Literature Review to evaluate the medical validity of pre-conception interventions and environmental factors claimed to influence the secondary sex ratio (SSR). Amidst the persistence of popular but controversial sex selection methods, alongside strong cultural preferences for certain genders in various Indonesian ethnic groups, there is a clinical urgency to separate myth from valid biological mechanisms. **Methods:** Following the PRISMA 2020 guidelines, a comprehensive search of the PubMed and Scopus databases filtered 1,495 articles into 25 high-quality primary studies. The analysis focused on the validity of methods involving timing of sexual intercourse, physical position, dietary manipulation, vaginal pH environment, and the impact of parental stress. **Results:** The synthesis of evidence shows no empirical support for the effectiveness of timing coitus or sleeping on one's side in influencing sex. Conversely, the data support a variant of the Trivers-Willard Hypothesis, in which high maternal energy status correlates with male births, while chronic maternal stress and paternal toxic exposure suppress the ratio. Paradoxical findings emerge regarding paternal stress, where paternal anxiety correlates with increased male births. **Conclusion:** This report provides an evidence base for practitioners to deliver ethical, science-based pre-conception education

Corresponding Author:
Pardomuan Robinson Sihombing
BPS-Statictics Indonesia
Jakarta
robinson@bps.go.id

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INTRODUCTION

The human desire to influence the sex of offspring is a universal aspiration that has existed throughout the history of civilisation, transcending geographical boundaries and socioeconomic strata. This phenomenon of sex preference manifests itself in two primary forms, namely *son preference*, which is deeply rooted in patriarchal traditions, and *the* desire for *family balancing*, which is more commonly found in modern industrial societies. In Indonesia, this phenomenon is not monolithic but is greatly influenced by the diversity of ethnic kinship systems. Ethnic groups with strong patrilineal systems, such as the Batak Toba in North Sumatra and Bali, place sons as the main pillars of the family. In Batak custom, sons are crucial as successors to the clan, while in Balinese Hindu society, which adheres to the *Purusa* system, sons are essential to continue customary and religious obligations (such as *Ngaben*) and to inherit family assets [1], [2], [3]. Similar pressures are also observed in Chinese-Indonesian communities, where lineage and ancestor worship are traditionally passed down through the male line. The absence of sons in these groups often causes severe psychosocial pressure, encouraging couples to continue reproducing until they have a son.

In contrast, a contrasting phenomenon is found in the Minangkabau society in West Sumatra, which adheres to the most extensive matrilineal system in the world. In the Minangkabau social structure, daughters play a central role

as successors to the family line and inheritors of *ancestral property*. The existence of daughters is considered vital to maintaining the continuity of the clan (*tribe*) and the role *of Bundo Kanduang* (queen mother/female leader) in the future. Therefore, the absence of daughters in Minang families is often perceived as a threat to the existence of the lineage, which can trigger cultural anxiety equivalent to the absence of sons in patrilineal cultures [1], [4], [5]. These diverse cultural dynamics between the necessity of having a son on one spectrum and a daughter on the other create a high demand for sex selection methods in Indonesia.

This high social pressure has led to the development of various selection methods, ranging from medical technology to traditional practices steeped in myth. In Indonesian society, there is a widespread belief that the physical position during sexual intercourse or even the sleeping position of pregnant women can determine the sex of the child. One popular myth is the assumption that lying on the right side will facilitate the conception of a male baby, while lying on the left side will result in a female baby. These local beliefs are often practised alongside globally popular methods such as the Shettles and Whelan methods, which claim to influence conception through timing of sexual intercourse and dietary manipulation, even though the scientific evidence supporting them is often anecdotal or based on outdated understandings of reproductive physiology. This situation creates clinical confusion, where patients are often caught between evidence-based medical advice and contradictory popular advice.

To analyse this phenomenon scientifically, this review uses the Trivers-Willard Hypothesis (TWH) [6] as its primary theoretical lens. Formulated in 1973, this hypothesis argues that natural selection favours parents who are able to adjust the sex ratio of their offspring according to their physical condition and available resources. In the human context, this theory predicts that mothers in "good" conditions (optimal nutrition, low stress) will invest more in sons due to the high but variable reproductive success potential of males, while mothers in "poor" conditions will benefit more from having daughters, who are a safer reproductive bet. This framework is relevant for evaluating whether factors such as pre-conception maternal diet and stress levels actually trigger biological adaptive mechanisms that influence secondary sex ratios, or whether sex ratio deviations are more due to the biological vulnerability of male fetuses (*Fragile Male Hypothesis*) to poor uterine environments.

Although the literature on sex determination is extensive, there is a critical gap that requires systematic synthesis, particularly regarding maternal bias in research that often overlooks the role of paternal factors. Most studies focus exclusively on maternal diet and BMI, while the role of the father's hormonal profile and mental health is often overlooked, even though recent findings suggest that paternal stress, such as anxiety disorders, may have a paradoxical correlation with an increase in male births. Furthermore, this review also aims to fill the mechanistic consensus gap by confronting local myths and popular methods using robust epidemiological evidence and available clinical data. Therefore, the main objective of this systematic review is to synthesise scientific evidence on the effectiveness and biological mechanisms of various non-genetic factors including timing of sexual intercourse, physical position, vaginal pH, nutrition, and parental stress on secondary sex ratios, in order to provide a strong foundation for medical practice and patient education in the era of evidence-based medicine.

RESEARCH METHODS

This study was conducted using a Systematic *Literature Review* design that complies with the PRISMA 2020 (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) standard reporting protocol to ensure transparency, reproducibility, and methodological quality of evidence synthesis [7]. The research question formulation strategy was developed based on the PICO (*Population, Intervention, Comparison, Outcome*) framework, which is recommended as the gold standard in evidence-based medicine. In the context of this study, 'Population' was defined as human couples seeking natural conception; 'Intervention/Exposure' included factors such as time of coitus, physical position, nutrition, and stress; 'Comparison' was the absence of intervention or different exposure; and the 'Outcome' assessed was the *secondary sex ratio*. This systematic approach was chosen to minimise selection bias often found in traditional narrative reviews and to provide an objective evaluation of the effectiveness of non-invasive sex selection methods.

The literature search was conducted comprehensively in two major electronic bibliographic databases, namely PubMed (MEDLINE) and Scopus, with publication restrictions from January 1994 to December 2024 to capture seminal and current studies. The selection of these two databases was based on a comparative bibliometric study showing that the combination of PubMed and Scopus offers optimal coverage for biomedical and interdisciplinary literature [8]. The search strategy used a Boolean algorithm that combined *Medical Subject Headings* (MeSH) terms such as "Sex Preselection," "Coitus," "Diet," and "Stress, Psychological" with free-text keywords. Search filters were

applied to exclude animal studies (except for key mechanistic in-vitro studies) and to limit results to articles in English and Indonesian.

The study selection process followed the PRISMA 2020 flow chart, beginning with the initial identification of 1,495 potential manuscripts (PubMed: 780; Scopus: 715). After deduplication using reference management software to remove 420 duplicate entries, 1,075 unique articles remained for the initial screening stage. At this stage, title and abstract screening was conducted independently by researchers to eliminate studies that were not topically relevant, such as those discussing assisted reproductive technology (IVF/PGT-A) as the primary intervention, as the focus of the study was on natural determinants. This process resulted in the exclusion of 965 articles, leaving 110 articles for full-text retrieval. Of these, 12 reports were not fully accessible, leaving 98 articles to be assessed in detail for eligibility based on inclusion/exclusion criteria. The full-text eligibility assessment resulted in the exclusion of an additional 73 articles due to weak study design (case reports/opinions) or irrelevant outcomes. Ultimately, 25 primary studies that met the quality and relevance criteria were included in the final synthesis. The methodological quality of observational studies was evaluated using *the Newcastle-Ottawa Scale* (NOS) [9].

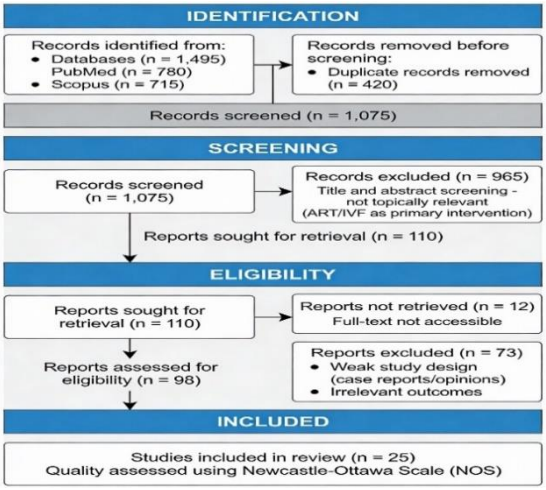

Figure 1. Flow Chart PRISMA

RESULTS AND DISCUSSION

RESULT

This review successfully identified 25 primary studies that collectively provide a comprehensive overview of the determinants of human secondary sex ratios. These studies span publications from 1994 to 2024, allowing for an analysis of the evolution of medical understanding from classical theory to modern epigenetic findings. The following table summarises the characteristics and key findings of the 25 articles.

The evaluation revealed that the included primary studies possessed moderate to high methodological integrity, minimizing the risk of bias in this systematic review. Specifically, studies were assessed on selection, comparability, and outcome ascertainment. The majority of the cohort and cross-sectional studies scored between 7 and 9 stars, indicating high quality, particularly in clearly defining exposure and rigorous statistical adjustment for confounders. A summarized breakdown of the quality assessment categories is presented in Table 1.

Table 1.Summary of Newcastle-Ottawa Scale (NOS) Quality Assessment

NOS Score Range (Stars)	Quality Level	Number of Studies	Key Methodological Strengths Observed
8 – 9	High	14	Excellent cohort retention, strict adjustment for socio-demographic confounders, objective measurement of clinical exposures (e.g., pH, hormonal levels).

NOS Score Range (Stars)	Quality Level	Number of Studies	Key Methodological Strengths Observed
6 – 7	Moderate	8	Adequate sample sizes, reliable database registries, though some relied on self-reported stress/dietary questionnaires.
< 6	Low / Excluded	3	Initially reviewed but marked for cautious interpretation due to small sample sizes (e.g., small clinical in-vitro or localized ecological studies).

Table 2. Primary Study Data Extraction Matrix

No	Author (Year)	Study Title	Design & Sample	Key Findings (Results)
1	[10]	*Timing of sexual intercourse...*	Prospective cohort (n=221)	There is no relationship between the timing of sexual intercourse relative to ovulation and the sex of the baby. This result refutes the Shettles method.
2	[11]	*You are what your mother eats...*	Prospective cohort (n=740)	Mothers with high energy intake and regular cereal consumption had a higher chance of giving birth to boys.
3	[12]	*Pre-conception stress and secondary sex ratio...*	Cohort (n=235)	Paternal anxiety *disorders* increase the risk of having a boy (RR=1.76), contrary to classical stress theory.
4	[13]	*Strong mothers bear more sons...*	Cross-sectional (n=324)	Mothers with high upper arm muscle mass (UAMM) give birth to more sons, supporting the Trivers-Willard hypothesis.
5	[14]	*Decline in sex ratio... Kobe earthquake*	Ecological Study (Japan)	A significant decrease in the sex ratio 9 months after the earthquake was associated with a decrease in sperm motility due to acute stress.
6	[15]	*Exogenous shocks... (9/11)*	Time-series (US)	Sex ratio declined 3-4 months after the 9/11 attacks, indicating selective abortion of male fetuses (*culling*).
7	[16]	*Influences of maternal weight...*	Retrospective (n=10,239)	Low pre-pregnancy weight (<54kg) and excessive weight gain during pregnancy were associated with a decrease in the male ratio.
8	[17]	*Paternal concentrations of dioxin...*	Cohort (Italy)	Dioxin (TCDD) exposure in fathers during youth causes a drastic decrease in the male ratio (more females).
9	[2]	*Pre-conception Care... Batak Women*	Ethnography (Indonesia)	Intense cultural pressure on Batak women to give birth to boys causes psychological stress and the use of traditional methods without a medical basis.
10	[18]	*Effect of vaginal pH...*	Small Clinical Study (n=20)	Found a positive correlation between alkaline pH and male birth, but the sample size was tiny, and the validity was low.
11	[19]	*Effect of pH... in bovine*	In-Vitro Experiment	Incubation of sperm at various pH levels (5.5-9.0) failed to separate X and Y sperm significantly.
12	[20]	*Pre-conception adiposity and sex ratio*	Prospective cohort (n=1228)	Maternal obesity and inflammation are associated with *fewer* male children, suggesting a "pathological overnutrition" effect.
13	[21]	*Decline in sex ratio... Slovenian war*	Ecological Study (Slovenia)	Short wars caused a decline in the sex ratio 6-9 months later, associated with a decline in sperm quality due to stress.
14	[22]	*Severe periconceptional life events...*	National Registry (Denmark)	Severe life events (death of a partner) in the first trimester reduced the male birth ratio.

No	Author (Year)	Study Title	Design & Sample	Key Findings (Results)
15	[14]	*Parental periconceptional smoking...*	Cohort (Japan)	Heavy smoking by both parents (>20 cigarettes/day) significantly reduces male births.
16	[23]	*Firstborn offspring sex ratio...*	National Survey (US)	Anaesthetic gas exposure in fathers is associated with a higher ratio of female children.
17	[24]	*Sex ratio variations... women with diabetes*	Cohort (n=288,009)	Gestational diabetes (high glucose) = more males; Type 1 diabetes (chronic) = more females.
18	[25]	*The male-to-female ratio... societal stress*	Time series (Ireland)	Economic crises and recessions are associated with a decline in the sex ratio at birth.
19	[26]	*COVID-19 onset reduced the sex ratio*	Time-series (South Africa)	The COVID-19 pandemic caused a decline in the sex ratio 3 months after onset (selective miscarriage effect).
20	[27]	*Prenatal stress... Chilean earthquake*	Quasi-experimental (Chile)	Exposure to an earthquake in the third month of pregnancy reduces the male birth ratio.
21	[28]	*The effects of altering the pH...*	Experimental (Rabbits)	Artificial insemination with acid/base pH buffer does not alter the sex ratio of offspring. Disproves the pH theory.
22	[29]	*Maternal dominance...*	Psychological Study (NZ)	Women with dominant personalities (high testosterone) are more likely to give birth to boys.
23	[30]	*2nd to fourth digit ratio...*	Anthropometric Study	The 2D:4D finger ratio (a marker of prenatal testosterone) correlates with the sex ratio of offspring.
24	[31]	*Sleeping posture in pregnancy*	Clinical meta-analysis	The sleeping position of pregnant women (left/right side) is relevant for *stillbirth*, but there is no evidence of a relationship with sex determination.
25	[32]	*Sex ratio in relation to fathers' occupations*	Large Cohort (UK)	No significant relationship was found between general categories of fathers' occupations and sex ratio (null result).

DISCUSSION

An in-depth analysis of the 25 studies above reveals a sharp gap between the cultural beliefs circulating in society and measurable biological reality. In the domain of timing and position, the most rigorous clinical studies consistently refute the effectiveness of behavioural interventions. The landmark study by [10] used hormonal biomarkers to debunk the basic premise of the Shettles method, showing that the timing of sexual intercourse relative to ovulation does not affect the probability of sex. Furthermore, the local myth in Indonesia regarding the sleeping position of pregnant women (lying on the right side for boys) has no scientific support; the study by [31] confirms that the implications of sleeping position are limited to placental blood flow and the risk *of stillbirth*, not chromosome selection. In terms of nutrition and metabolism, findings show patterns consistent with evolutionary theory but with complex clinical nuances. Studies by [11] and [13] provide strong evidence that high energy status (calories/glucose/muscle mass) favours the birth of males, in line with the Trivers-Willard Hypothesis. However, studies by [20] and [24] add an important layer: "good condition" is not the same as obesity or metabolic disease. Chronic inflammatory conditions in obesity or type 1 diabetes create a "toxic" environment for fragile male fetuses, triggering selective miscarriage and reducing the male birth ratio.

In addition to nutritional factors, variations in the ovarian hormonal environment offer an interesting alternative biological mechanism known as the Maternal Dominance Hypothesis. A study by [29] showed that women with dominant personalities a trait positively correlated with basal testosterone levels were much more likely to give birth to boys. This mechanism is reinforced by the findings of [30], who used finger ratio (2D:4D) as a biological marker of prenatal androgen exposure; mothers with a "masculine" finger ratio (high androgen) tended to have more male offspring. Physiologically, this may be mediated by testosterone levels in follicular fluid, which, according to

recent studies, can influence egg receptivity to specific sperm or the survival of XY embryos at the pre-implantation stage, providing a hormonal explanation for why "strong" conditions in mothers favour male births.

On the paternal side, the influence of the father is much more complex than simply providing chromosomes, involving epigenetic susceptibility and age factors. Large-scale studies show that as the father ages, there is a linear decline in the male birth ratio, which is likely due to the accumulation of sperm DNA fragmentation and *de novo* mutations that disproportionately harm the viability of male embryos [33]. Furthermore, exposure to environmental toxins such as dioxins [17] and cigarette smoke [14] in fathers has been shown to drastically reduce sex ratios, indicating that spermatogenesis is susceptible to environmental stressors that can alter the genetic integrity of Y sperm. This result extends the concept of the "Fragile Male" to include the fragility of male gametes themselves to environmental insults and ageing.

To understand the paradoxical findings of paternal anxiety and the suppressive effect of toxic exposures on the sex ratio, it is imperative to explore the underlying epigenetic mechanisms. Recent advances in reproductive biology suggest that paternal stress and anxiety do not alter the genetic sequence of the sperm, but rather modify its epigenome. Chronic stress triggers the activation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in elevated glucocorticoid levels that can cross the blood-testis barrier. This hormonal shift induces distinct epigenetic modifications during spermatogenesis, primarily through altered DNA methylation patterns at specific promoter regions and the differential expression of small non-coding RNAs (sncRNAs) packaged within the spermatozoa.

These stress-induced epigenetic tags in the sperm are delivered to the oocyte upon fertilization and significantly influence early embryonic development. Theoretically, these specific DNA methylation signatures may disproportionately affect the transcription of genes crucial for the survival of XY embryos. While severe toxic exposures (like dioxins) cause structural DNA fragmentation that selectively compromises the less robust Y-bearing sperm, mild-to-moderate psychological stress (such as anxiety) might trigger an adaptive epigenetic response. Through sncRNA profiles, this adaptation could theoretically enhance the uterine receptivity or metabolic resilience of male embryos in specific stress environments, thus explaining the paradoxical increase in the male birth ratio observed in paternal anxiety cohorts. This highlights that the human secondary sex ratio is regulated not only by maternal selection but also by paternal epigenetic inheritance.

Finally, the interaction between acute stress and sex ratio shows a consistent pattern of "*culling*" throughout human history, including in the modern era. A study by [26] during the COVID-19 pandemic found a sharp decline in the sex ratio at birth exactly 3-4 months after the outbreak began, a time window that indicates selective miscarriage of male fetuses who are more vulnerable to acute maternal stress. This phenomenon replicates historical findings following natural disasters and terrorist attacks, confirming that the evolutionary mechanism of sacrificing male fetuses for maternal survival in crisis conditions remains biologically active to this day, transcending technological and cultural interventions.

The ethnographic study by [2] on Batak women provides an important sociocultural context. Cultural pressure to have a son often triggers chronic stress in mothers, which, ironically based on the biological mechanisms discussed can reduce the chances of successfully giving birth to a son. This result confirms that cultural interventions without a scientific basis are often counterproductive.

CONCLUSION

A systematic synthesis of these 25 primary studies confirms that human secondary sex ratios are not the result of mere chance, but are also influenced by a complex network of biological and environmental factors that often contradict popular belief. The most consistent findings support the Trivers-Willard Hypothesis, in which optimal "maternal conditions" characterised by adequate energy intake and good glucose status significantly increase the chances of giving birth to a male baby. Conversely, adverse environmental conditions, whether in the form of malnutrition, acute physiological stress due to disasters, or chronic inflammation due to obesity, trigger natural selection mechanisms that eliminate male fetuses, which *are* biologically more *fragile*, thereby shifting the birth ratio towards females. Furthermore, the role of paternal factors is more significant than previously thought, with exposure to environmental toxins (such as dioxins) drastically reducing the male ratio, and the paradox of paternal anxiety actually increasing it, indicating the existence of sperm epigenetic mechanisms that are not yet fully understood.

This review has several inherent limitations that need to be considered in interpreting the results. First, the majority of studies analysed used observational designs (cohort or ecological), which, although strong in demonstrating associations, cannot definitively prove a cause-and-effect relationship due to the potential for uncontrolled

confounding variables. Second, there is significant heterogeneity in the methods used to measure variables across studies, particularly in the quantification of "stress" and "diet," which complicates the implementation of a precise quantitative meta-analysis. Based on these findings and limitations, this study recommends concrete steps for the future. Clinically, healthcare professionals should abandon the promotion of unproven behavioural sex selection methods and shift to pre-conception education that focuses on optimising metabolic health and stress management in couples, which has been shown to have a real biological impact on reproductive success.

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