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Systematic Review

Fetal sex and its relationship with maternal health and pregnancy outcomes: a systematic review

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ABSTRACT

The role of fetal sex in maternal physiology has been understudied despite the evidence that sexually differential placental gene expression influences maternal metabolic, inflammatory, and hormonal regulation. This systematic review aims to examine how fetal sex influences maternal physiological responses and pregnancy-related complications, with a focus on hormonal regulation, immune function, and metabolic changes. By reviewing the existing literature, this study seeks to highlight the biological mechanisms underlying sex-specific maternal health risk. We made a comprehensive literature search using Google Scholar, PubMed, and Medline engine. Using a systematic filtering process, we included 17 articles in the analysis. The selected studies were analyzed to identify the impact of fetal sex on maternal physiology. It appeared that there are three key domains of maternal physiology (maternal hormonal regulation, immune function and metabolic adjustment and pregnancy-related health complications) that are influenced by the fetal sex. For example, out of the selected 17 studies, four revealed how the sex of a fetus regulates maternal hormonal levels, three indicated maternal inflammatory responses may to fetal-sex, showing differences in pro-inflammatory cytokine levels. The rest of the 10 studies revealed how fetal sex influences metabolic adjustments and maternal health complications. We concluded from the study that fetal sex is a significant biological determinant of maternal health. Considering the high risk of maternal morbidity and mortality among women of low and middle-income countries, ethnic specific studies are required to be conducted from the perspective of public health.

Keywords: Fetal sex, Maternal physiology, Placenta, Systematic review, Pregnancy-related health complications

INTRODUCTION

Pregnancy is a very specific and complex period in a woman's life.[1] Nearly 30% of all women experience an adverse pregnancy outcome.[2] Several factors including poor maternal nutrition, psychosocial stress, substance abuse, and environmental exposures contribute to adverse pregnancy outcomes, however, the placenta and the fetus serve as important determinants of maternal and fetal health during gestation.[3-6] Growing evidence suggests that signals generated by placenta and fetus have been linked to risk of obstetric complications.[7] The placenta of a fetus, functions as both an endocrine and immunomodulatory organ, with gene expression patterns that differ according to fetal sex.[8] Sex-specific placental biology is characterized by differential expression of a wide range of genes, including both sex-linked and autosomal genes, which may influence variations in maternal immune responses, hormonal regulation, and metabolic adaptations during pregnancy.[9] For example, genes related to immune pathways such as Janus Kinase 1 (JAK1), Interleukin-2 Receptor Subunit Beta (IL2RB), Clusterin (CLU), and Tumor Necrosis Factor Receptor (TNFR) are found to be showed elevated expression in females placenta compared to that in males. Variations in the Immune gene expression may be involved in the sexual dimorphism in maternal-fetal signaling and variations in maternal inflammation, stress reactivity, and metabolic regulation.[10,11] Studies showed that Fetal sex may differentially influence maternal hormonal adaptations, cortisol and blood pressure levels, immune responses, cardiovascular function and metabolic adjustments.[8,12,13] For instance,

variations in the production of cortisol can result from the maternal hypothalamus pituitary adrenal (HPA)-axis being influenced by the variable placental function based on fetal sex.[11,14]

The total cortisol levels in maternal serum during the first and second trimester of pregnancy vary with fetal sex.[14,15] For example, women who bear a female fetus exhibit more pronounced maternal inflammatory reactivity under immune challenge, reflecting stronger adaptive immune response.[16] Scholars like Jasienska argued that women who gave birth to more numbers of male offspring experience higher level of pro-inflammatory cytokines even many years after childbirth.[17] This perhaps implies that fetal sex can have persistent impact on the maternal immune system. Male fetus may contribute to the maternal immune system to become more pro-inflammatory throughout pregnancy, possibly as a result of sex-specific placental signaling, variations in fetal antigen exposure, and changes in the maternal immunological tolerance.[18] A long-term immunological adjustment in the mother may result from repeated exposure to this enhanced inflammatory state during pregnancies involving male fetuses.[8,18] As a result, these sex-specific immunological interactions, which are mostly mediated through the placenta, may accelerate immune aging and raise long-term maternal health risks by contributing to a persistent, low-grade inflammatory state, which is a characteristic of inflammaging.[16,19]

Evidence from epidemiological studies has shown that women who are pregnant with male fetus sex has been associated with an increasd risk of gestational diabetes, placenta previa, preeclampsia, and hypertension, all of which may influence women's health beyond pregnancy.[19,20] It has been consistently demonstrated that carrying a male fetus increases the risk of macrosomia, possibly as a result of higher rates of fetal development and sex-specific placental modifications that promote nutrient transfer and growth.[21] A community-based cohort study involving a large population combined with a meta-analysis reported that Male-bearing pregnancies were significantly more prone to be complicated by placenta previa. The meta-analysis indicated a 14% higher risk of placenta previa among male-bearing pregnancies, indicating that male fetal sex may be associated with abnormal placentation.[22] A systematic review and meta-analysis involving over 3 million pregnancies found that male fetal sex was related to an increased risk of preeclampsia/eclampsia in non-Asian populations.[23] Whereas a large-scale study involving 219,575 pregnancies from global cohorts reported that preterm preeclampsia shows a higher frequency in pregnancies with a female fetus.[24] A study investigating maternal immune markers demonstrated that pregnancies carrying female fetuses exhibited distinct inflammatory and regulatory cytokine patterns. Female fetal sex was related to elevated levels of several regulatory cytokines, indicating sexual dimorphism in maternal immune adaptation during pregnancy.[25]

The relationship between fetal sex and maternal physiology has been understudied in both clinical and epidemiological studies around the world. This gap may limit our understanding of the complex biological interactions that occur during pregnancy. Identifying fetal sex as a crucial biological factor is therefore important, not only for identifying sex-specific vulnerabilities of maternal physiology but also for guiding the development of more precise, personalized obstetric care. In countries like India, where prenatal sex determination is illegal due to ethical and social concerns surrounding sex-selective abortion practices, studies exploring fetal sex differences may be particularly sensitive.[26] As a result, this area of research often faces skepticism, despite its potential scientific value in understanding sex-specific maternal physiological adaptations. In many developed nations like the United States and the UK, fetal sex disclosure during pregnancy is legally permitted and commonly practiced, often marked by social celebrations. Despite this accessibility and clinical relevance, research examining the impact of fetal sex on the maternal physiology and health complications remains limited.

This systematic review is an attempt to synthesize the evidence from observational and cohort studies, and highlighting this underexplored dimension of maternal health.

Literature search

Data sources and search strategy

A stepwise literature search was done between August 2025 and February 2026. In the first phase, relevant articles were identified using electronic databases and search engines, including Google Scholar, PubMed and MEDLINE. Search terms included “fetal sex,” “maternal health,” “maternal physiology,” “maternal health complications,” “maternal hormones,” “placental function,” “fetal–maternal interaction,” “preeclampsia,” and “gestational diabetes.” Boolean operators were applied to combine search terms, including (“fetal sex” OR “offspring sex”), (“maternal health” OR “maternal physiology”), and (“placental function” AND “pregnancy complications”). In the second phase, the reference lists of the initially selected articles were reviewed to locate further relevant studies. Finally, the selected literature was critically assessed to identify the existing research gaps and areas requiring further investigation.

Selection criteria

This review included studies that discussed about the association between fetal sex and maternal physiological changes, such as hormonal regulation, immune function, placental biology, and metabolic adaptations, or pregnancy-related complications (e.g., gestational diabetes mellitus, preeclampsia, and gestational hypertension). Only studies published between 2000 and 2025, written in the English language, and published in journals indexed in

databases such as PubMed, ResearchGate, and Google Scholar were considered for inclusion.

Data extraction and screening process

Both the authors independently screened the titles, the abstracts, and the full text articles that fulfilled the inclusion criteria. Relevant data were extracted from the selected articles using a structured approach. For example, from each of the selected articles, we gathered information on the year of publication, study design (e.g., cohort, cross-sectional, experimental), population characteristics (including sample size and geographical location), and the specific maternal outcomes assessed in relation to fetal sex. The key variables considered were maternal physiological indicators such as blood pressure, cortisol levels, immune responses, and metabolic parameters, as well as pregnancy-related complications such as gestational diabetes, preeclampsia, and gestational hypertension. These articles were also examined for the evidence on hormonal regulation, inflammatory markers, and sex-specific placental function. We eliminated articles which did not directly assess fetal sex-specific maternal outcomes, those published in non-English languages, and as editorial letters or book reviews. We finally considered 17 research articles available in full text that explored the impact of Fetal Sex on Maternal Health for this review (Figure 1).

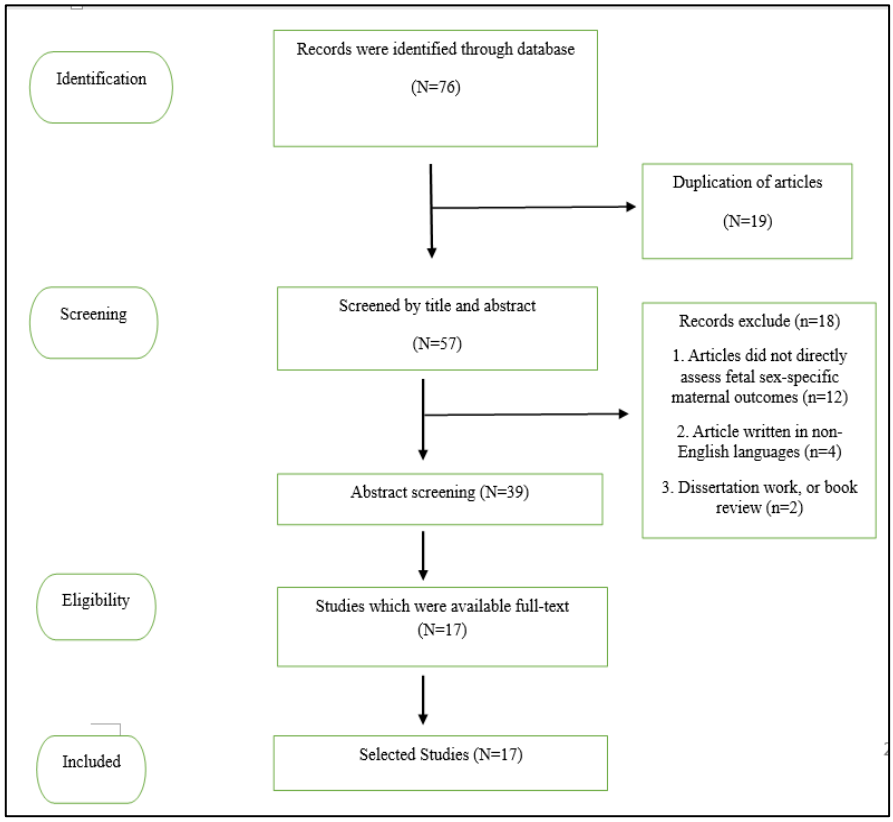


Figure 1: Indicate the process of study selection.

Quality assessment

We evaluated the methodological quality of the chosen studies. The study's quality and topic relevance were identified using a quality assessment tool which was adopted from McFadden et al.[27] Based on selection bias, study design, data collection method, and confounding factors, the cataloguing system for quantitative studies was divided into "low risk," "moderate risk," and "high risk" categories.

Review articles were assessed according to their findings, methodological clarity, number of studies reviewed, and topic relevance. These standards were used to further classify the articles' quality as "strong," "moderate," and "weak."

The Preferred Reporting in Systematic Reviews and Meta-analyses (PRISMA) Guidelines were followed when reporting the findings.[28]

Methodological quality of included studies

According to the prepared catalogue of risk assessments, six of the quantitative studies were considered to be of moderate risk, and five of low risk. Among the review articles, four were rated as strong, one as moderate, and one as low quality (Tables 1 and 2).

Table 1: The methodological quality of chosen quantitative studies.

Study	Nature	Sample size	SB	SD	DC	C	OR
Tamimi et al 2003	Cross-sectional	244	L	L	L	L	L
Al Atawi et al 2005	Observational longitudinal	36	M	M	L	M	M
DiPietro et al 2011	Prospective observational cohort	165	L	L	L	M	L
Aibar et al 2012	Retrospective cohort	2000	L	M	M	M	M
Weissmann-Brenner et al 2015	Retrospective cohort	37237	L	M	M	M	M
Enninga et al 2015	Observational longitudinal cohort	38	M	M	M	M	M
Mitchell et al 2017	Observational	80	L	M	M	M	M
Taylor et al 2018	Case-control study	648	L	L	L	L	L
Galbarczyk et al 2019	Cross-sectional	559	L	L	L	M	L
Cowell et al 2021	prospective cohort	874	M	M	M	M	M
Vrijkotte et al 2023	Analytical observational	3049	L	L	L	L	L

*Developed by authors based on quality assessment done by following catalogue developed by McFadden et al. SB: Selection bias, SD: Study design, DC: Data collection method, C: Confounding, OR: Overall risk, H: High risk, M: moderate risk, L: Low risk

Table 2: The methodological quality of review articles.

Study	Nature	Sample size	Quality assessment
Mondal et al 2014	Systematic review and meta-analysis	30 million	Strong
Jaskolka et al 2016	Systematic review and meta-analysis	3163735	Strong
Schalekamp-Timmermans et al 2017	Meta-analysis	219,575	Strong
Al-Qaraghouli and Fang 2017	Narrative review	NA	Weak
Broere-Brown et al 2020	Systematic review and meta-analysis	74 individual study	Moderate
Jasienska, 2020	Narrative review	NA	Strong

*Developed by authors based on quality assessment done by following catalogue developed by McFadden et al.

Table 3: General findings of the studies included in the review.

Factors affecting by fetal sex	Studies	Findings
Hormonal regulation	Al Atawi et al, DiPietro et al, Jasienska et al, Vrijkotte et al	Leptin levels were significantly higher during all three trimesters in the pregnant women carrying a female fetus in comparison with male fetus. At the start of pregnancy, Women with male fetuses had significantly higher cortisol levels, but after 30 weeks, women carrying female fetuses showed higher cortisol levels until delivery. Women pregnant with a male fetus have different cortisol levels and diurnal cortisol patterns. Women pregnant with a female fetus had higher maternal total cortisol levels.
Immune function	Enninga et al, Mitchell et al, Taylor et al	Male fetus was associated with higher levels of proinflammatory cytokines (G-CSF, IL-12p70, IL-21, and IL-33) and angiogenic factors. Pregnant women with a female fetus showed a stronger inflammatory immune response throughout pregnancy compared to those carrying males. Women carrying female fetuses showed different levels and patterns of cytokines (such as IL-1β, IL-6, IL-10, IFN-γ, etc.) compared to women carrying the male fetuses.

Continued.

Factors affecting by fetal sex	Studies	Findings
Metabolic adjustments and health complications	Tamimi et al, Aibar et al, Mondal et al, Weissmann-Brenner et al, Jaskolka et al, Schalekamp-Timmermans et al, Al-Qaraghouli and Fang et al, Galbarczyk et al, Broere-Brown et al, Cowell et al	Women carrying male rather than female embryos may have higher energy requirements and that male embryos may be more susceptible to energy restriction. Male fetal sex independently contributes to the risk of adverse obstetric and perinatal outcomes. Male fetuses have a higher risk of stillbirth, posing additional maternal health risks and contributing to greater reproductive burden. As maternal age increased, pregnancies involving male fetuses exhibited a higher risk of hypertensive disorders. Male fetus was associated with increased maternal risk of pre-eclampsia/ eclampsia. Sexual dimorphic differences in the occurrence of preeclampsia exist, with preterm preeclampsia being more prevalent among pregnancies with a female fetus as compared with pregnancies with a male fetus. Male fetus has been associated with a higher risk of preterm labor, labor complications, umbilical cord abnormalities, increased cesarean delivery, greater heart rate variability, and a higher likelihood of gestational diabetes due to reduced beta-cell function. Having more sons, but not daughters or total children was linked to poorer self-rated health; the odds of poor health increased by 11% with each additional son. Pregnancy complications (i.e., gestational hypertension, gestational diabetes, total pre-eclampsia, eclampsia, placental abruption, and post-partum hemorrhage) tended to be associated with a male fetus, except for preterm pre-eclampsia. During the postnatal period, women who were pregnant with a male fetus were far more likely to experience depressive symptoms.

DISCUSSION

Fetal sex, metabolic adaptations, and maternal health complications

Among the 17 studies selected for review, 10 were focused only on metabolic adjustments and maternal health complications influenced by fetal sex. Here, metabolic adjustment and health complications refer to energy requirement, gestational hypertension, diabetes, preeclampsia, depressive symptoms. The findings reveal that male fetus is more frequently linked to adverse maternal health outcomes, although certain complications such as preterm preeclampsia were reported more often in women carrying a female fetus. Among the 10 studies, three examined associations between fetal sex and maternal risk of pre-eclampsia. Preterm preeclampsia was more prevalent among those who were pregnant with a female fetus, while pregnancy with a male fetus was associated with increased risk of term pre-eclampsia, and eclampsia. Among the three studies analyzed, two were systematic reviews and meta-analyses, while one was only meta-analysis. These studies aimed to explain why the risk of preeclampsia and eclampsia differs according to fetal sex. The placenta contributes significantly to a significant involvement in these differences since it shows sex-specific patterns of gene expression, hormone production, and immune activity.[10] The placenta of a male female grows rapidly to improve fetal growth, but it has less capacity to adapt when exposed to either maternal stress or with reduction of uterine blood flow. This might result in the increase in the likelihood of 'term preeclampsia', when maternal hypertension tends to occur during the later period of pregnancy. In contrast, the placenta of a fetus shows greater plasticity and immune regulation. It prioritizes maternal survival, by adjusting growth and metabolic pathways when the intrauterine environment becomes unfavorable. However, these adaptive responses may contribute to preterm preeclampsia, when pregnancy terminates earlier to protect maternal health. Among women with eclampsia, where seizures occur following preeclampsia, similar mechanisms are contributing to oxidative stress, systemic inflammation, and endothelial dysfunction. Since these are partially modulated by placental hormones and cytokines, fetal sex-specific placental signaling may also influence the severity or

timing of eclamptic symptoms include generalized seizures, severe headache, visual disturbances, altered mental status, hyperreflexia, epigastric or right upper quadrant pain, and loss of consciousness.[8,10,12,24,29,30]

The remaining seven studies examined the differential impact of fetal sex on maternal physiology. But each of these studies focused on the distinct aspects of this relationship. For example, some studies explored the differential energy requirements of the mother with respect to fetal sex. Other studies explored the differential effect of fetal sex in the maternal metabolic and, psychological outcomes, and pregnancy complications such as gestational diabetes or hypertension. These results collectively imply that fetal sex may have an impact on maternal physiology through multiple biological pathways, contributing to sex-specific risks during and after pregnancy. A study done in China and the United States found that women carrying male fetuses linked to approximately 10% greater energy requirements than those carrying female fetuses, indicating that male fetuses more frequently linked to increased energetic demands and can influence maternal physiology. A rapid growth and higher metabolic demands of the male fetus require greater maternal energy and nutrient supply. When maternal energy intake is limited, the male fetus is less able to adapt to the reduced resources, becomes more vulnerable to growth restriction and even to fetal death; female fetus tends to be more resilient under nutritional stress.[31] Corroborating with this finding, a systematic review and meta-analysis based on 30 million births worldwide also revealed that male fetus` are 10% at a higher chance of stillbirth compared to female fetuses, a pattern consistent across countries, ethnicities, and time span.[32] Male fetus appears to increase maternal health risks, and this effect can continue into the postnatal period. A study conducted in Poland found that after adjusting for the factors such as age, education, marital status, smoking habit, and body mass index, the likelihood of reporting poor health increased by 11% with each subsequent son born.[19] This suggests that bearing a male fetus may be associated with increased long-term physiological and energetic demands on mothers, potentially contributing to accelerated decline in health over time. Cowell et al showed that male fetal sex was associated with significantly higher odds of experiencing depressive symptoms during the postnatal period.[7] This association may be linked to sex-specific differences in maternal immune and hormonal responses during pregnancy. Women who have pregnant with a male fetus experienced higher maternal inflammation and variation in cortisol regulation. These changes can adversely affect the hypothalamic-pituitary-adrenal (HPA) axis and influence maternal emotional well-being after birth.[12]

Fetal sex also plays an important role in determining the risk of unfavorable pregnancy outcomes.[20] For instance, male fetus has been associated to a greater chance of preterm labor, development of abnormalities in the umbilical cord (such as nuchal cord or cord prolapse), and an increased likelihood of cesarean delivery. Women carrying a male fetus are prone to show heightened vulnerability in heart rate and at a higher risk of gestational diabetes mellitus (GDM), possibly due to reduction of pancreatic β-cell function and insulin sensitivity with male pregnancies. These differences are thought to reflect sex-specific variations in the placental function, hormone production, and immune responses, and how the maternal body responds and adapts to the metabolic, endocrine, and immunological demands of pregnancy.[13,33]

Fetal sex and maternal immune function

Maternal immune changes during pregnancy involve intersectionality of a number of factors (hormones, stress, nutrition, infections). Thus, it is difficult to isolate the effect fetal sex in particular on maternal immune system. As a result, evidence on maternal immune modulation by fetal sex remains limited, and often inconsistent. Since the maternal immune system plays the central role nearly in every aspect of pregnancy, including implantation, placental development, maternal immune tolerance to the fetus, and protection against infection, a nuanced understanding of how fetal sex influence maternal immune function is important. A shift in maternal immune activity due to fetal sex may elevate a chance of pregnancy complexity such as preeclampsia, gestational diabetes, preterm birth, postpartum depression, and infections.[12,16,23,25,34] Immune changes during pregnancy also affect long-term maternal health, including inflammation-related diseases, metabolic disorders, and postpartum recovery period. The maternal immune system is largely dependent on cytokines, which are small signaling proteins that help immune cells communicate with each other. They regulate inflammation, immune tolerance, tissue repair, and defense against infections. During pregnancy, the cytokine level requires precise balance to protect the mother while maintaining tolerance to the fetus.

The only three existing literature that dealt with maternal immune system and maternal health focused on whether the levels of pro-inflammatory cytokines differ by fetal sex, indicating that maternal inflammatory responses may be sex-specific. For example, a study done in Minnesota showed that male fetus is likely to have a higher level of pro-inflammatory cytokines (G-CSF, IL-12p70, IL-21, and IL-33) and angiogenic factors compared to that of the female fetus. This indicates the maternal immune and vascular systems respond differently depending on the fetal sex, possibly contributing to the variations in maternal physiology.[12] Another US based study demonstrated that woman carrying a female fetus exhibited different levels and trajectories of key cytokines including IL-1β, IL-6, IL-10, and IFN-γ in comparison with those carrying a male fetus. This highlights the concept that immune regulation during pregnancy is influenced by fetal sex, with male and female fetus shape the maternal cytokine responses in distinct ways.

Fetal sex and maternal hormonal regulation

We also identified four studies that reveal how the sex of a fetus regulates maternal hormonal levels. The endocrine environment during gestation period, particularly the levels of cortisol, leptin, and placental hormones can vary with the fetal sex. Sexual dimorphism hormonal patterns indicate how the fetus actively contributes in shaping maternal physiology, leading to the differences in metabolic regulation, stress responses, and immune functioning across pregnancy.[14,15,35] An US based study showed that regardless of the ethnic background, pregnancy with female fetus increases the salivary cortisol concentrations relative to those pregnant with a male fetus during late pregnancy. The authors of this study argued that there is a sex-specific placental regulation of cortisol metabolism, as the placenta modulates maternal-fetal glucocorticoid transfer through enzymes such as 11β-HSD2.[15] Three studies in this category, showed similar pattern regarding variation in the maternal hormonal regulation with fetal sex. For example, Al Atawi et al found that maternal leptin levels are consistently higher across all the three trimesters among those pregnant with a female fetus compared with those pregnant with a male fetus.[35] This difference may be partly driven by estrogen-related regulation, since estrogen enhances leptin production.[36] Higher leptin levels also reflect sex-specific placental function; female placentas tend to show greater endocrine and metabolic activity. Since leptin plays the central role in energy regulation, an elevated maternal leptin level may represent an adaptive response that supports the more energy-efficient growth patterns typical of a female fetus. Together, these mechanisms underline how placental gene expression and hormone production differ by fetal sex, shaping maternal metabolic physiology throughout the pregnancy period.[10] Similarly, a study conducted in Europe found that women who are pregnant with a female fetus had higher maternal total cortisol levels in comparison to those pregnant with a male fetus. These findings indicate that fetal sex may impact maternal stress-response system during pregnancy. One explanation is that the female placenta may regulate cortisol metabolism differently, allowing more maternal cortisol to circulate. The placenta controls cortisol transfer using enzymes such as 11β-HSD2, and sex-specific differences in this enzyme's activity may lead to higher cortisol in a woman pregnant with a female fetus. Elevated cortisol in these pregnancies may reflect a more reactive or adaptive maternal-placental endocrine environment.[8,14] Overall, the evidence suggests that sex-specific placental biology and metabolic signaling contribute differential maternal health burdens.

Population variation, placental adaptation, and reproductive costs

The association between fetal sex and maternal health outcomes is not entirely consistent across populations, suggesting that biological, environmental, and socio-cultural factors may modify these associations.[20,32] Variations in maternal nutritional status, ethnicity, healthcare access, maternal age, parity, and genetic background may influence the extent to which fetal sex affects maternal physiology. From an evolutionary perspective, these findings may be interpreted within the framework of parental investment and life-history theory. Male fetuses generally exhibit faster growth and greater energetic demands, requiring increased maternal investment during gestation. In contrast, female fetuses appear to adopt more flexible developmental strategies that enhance survival under adverse intrauterine conditions.[10,29] The placenta is likely a key mediator of these differences. Evidence indicates that male and female placentas differ in gene expression, endocrine activity, immune regulation, and responses to environmental stressors. Male placenta tend to prioritize fetal growth, whereas female placentas exhibit greater adaptive plasticity under suboptimal conditions.[10,13] The implications of these findings may extend beyond pregnancy. Greater energetic and inflammatory demands associated with certain pregnancies could contribute to the cumulative physiological costs of reproduction, potentially influencing maternal health and ageing trajectories over the life course.[7,19,29]

Thus, it appears from the above discussion that fetal sex influences maternal health outcomes. But, data on this particular topic across the global population is limited. This gap is particularly notable in countries like India where there is a large share of stillbirths 9.7 per 1,000 births, and maternal health remains a significant public health burden emphasizing the need for improved surveillance and intervention strategies.[37,38] It would be also interesting to examine whether fetal sex specific maternal outcomes are universal or ethnic specific, parity specific and dependent on maternal age and antepartum care.

Implications

In countries where prenatal sex identification is legally prohibited (like India, China), the sex-specific physiological costs of reproduction become apparent only after delivery. Given the potentially greater energetic demands associated with the gestation and birth of male offspring, mothers delivering male infants may require increased attention to postpartum recovery and nutritional support.

The relationship between fetal sex and maternal physiology highlights the need for further research into sex-specific maternal health outcomes. Such investigations are significantly important in countries where prenatal sex determination is legally prohibited, which help to address this problem through improved postpartum care strategies.

Fetal sex can be identified through ultrasonographic assessments by healthcare professionals, after approximately the 11th to 12th week of pregnancy. Knowledge of sex-specific maternal physiological

responses may enhance more individualized maternal care without revealing the fetal sex to the parents, thus maintain consistency with existing legal standards.

Limitations

The restricted number of eligible studies highlights the existing gap in research exploring sex-specific differences in maternal health during pregnancy. A larger number of studies would have supported for stronger and comprehensive findings with community-specific variations. The impact of fetal sex on maternal immune function is particularly underreported. This gap is relevant considering the central role of immune regulation in ensuring pregnancy progression, facilitating maternal–fetal tolerance, and determining both short- and long- term maternal health outcomes.

CONCLUSION

This systematic review highlights fetal sex as a significant biological determinant influencing maternal physiology and pregnancy outcomes. The evidence suggests that there is an association between hormonal regulation, immune responses, metabolic adaptations, and susceptibility to pregnancy-related complications. Mostly, male fetal sex was more frequently associated with adverse maternal outcomes, including gestational diabetes, hypertensive disorders, increased energetic demands, and postpartum depressive symptoms, although certain conditions, such as preterm preeclampsia, appeared to be more common in pregnancies involving female fetuses. These sex-specific differences are controlled by variations in placental gene expression, endocrine activity, immune signaling, and maternal–fetal interactions. Such mechanisms may influence maternal stress responses, inflammatory processes, and metabolic regulation during pregnancy. The findings emphasize the importance for further research across diverse populations, especially in developing countries where maternal morbidity and adverse pregnancy outcomes remain major public health concerns.

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