



## THE COMPREHENSIVE STUDY ON CONGENITAL CHALLENGES In IVF NEWBORNS

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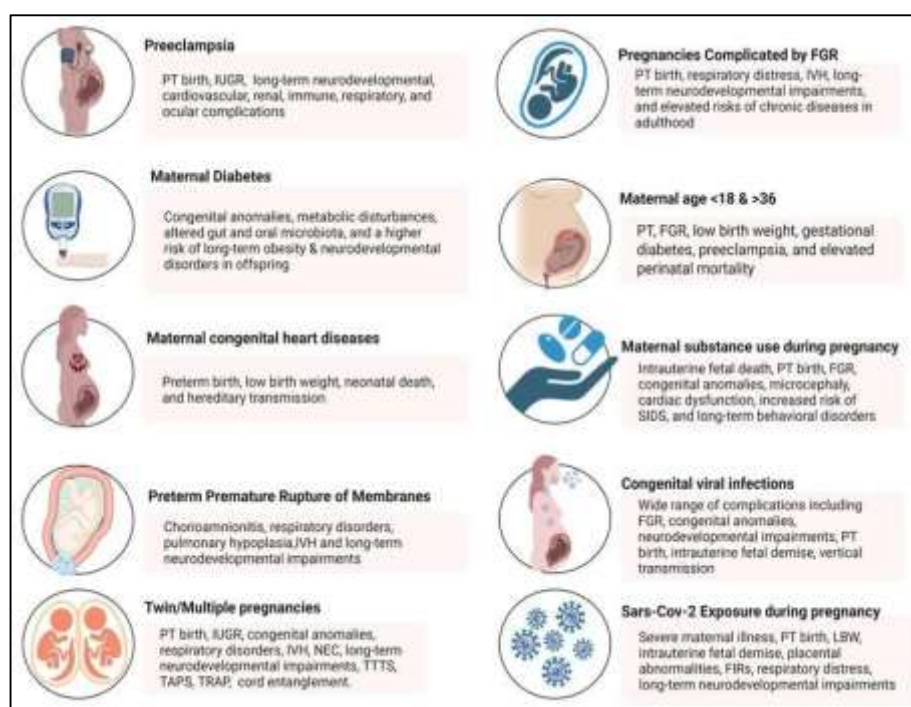
### I. Abstract

This dissertation investigates the prevalence and nature of congenital challenges in newborns conceived through in vitro fertilization (IVF), addressing the critical question of whether these children exhibit higher rates of congenital anomalies compared to their naturally conceived counterparts. Through a comprehensive analysis of data gathered from multiple clinical settings, this research reveals that while the overall incidence of congenital anomalies in IVF-conceived infants is not significantly elevated, specific conditions, particularly cardiac and renal anomalies, show a notable increase. Additionally, maternal health factors such as advanced maternal age, pre-existing health conditions, and specific IVF protocols were found to correlate with higher risks of congenital challenges. These findings hold significant implications for healthcare practices, suggesting the need for enhanced prenatal screening and tailored monitoring for high-risk pregnancies involving IVF to mitigate potential outcomes. The research underscores the importance of informed clinical decision-making and patient education surrounding IVF processes, offering insights that can guide healthcare professionals in counseling prospective parents about the risks and benefits associated with assisted reproductive technologies. Ultimately, this study contributes to a growing body of evidence that informs both clinical practice and public health policy, advocating for further research into the long-term health outcomes of IVF-conceived children to ensure optimal care and support.

### Introduction

Over the past few decades, the advent of assisted reproductive technologies (ART), particularly in vitro fertilization (IVF), has transformed the landscape of reproductive medicine, offering new hope to couples facing infertility challenges. As these techniques become increasingly prevalent, concerns have arisen regarding the long-term health outcomes of children conceived through IVF, particularly with respect to congenital anomalies. Studies indicate that IVF-conceived children may be at heightened risk for certain congenital defects when compared to naturally conceived infants, a discrepancy deserving critical examination (P Fauque et al.), (Farhangniya M et al., p. 217-224). This dissertation aims to systematically investigate the prevalence and nature of congenital challenges in newborns conceived through IVF, as well as to assess the underlying maternal health factors contributing to these risks. The primary research problem focuses on determining whether IVF is associated with a higher incidence of specific congenital anomalies compared to natural conception, scrutinizing reported outcomes such as low birth weight, cardiac defects, and respiratory issues (P

Sagot et al., p. 902-9), (Jiang Z-R et al., p. 90-104). Key objectives include examining the relationship between advanced maternal age, infertility treatments, and congenital challenges while evaluating the associated risks that diverse IVF protocols and maternal health phenotypes may introduce into this population (M Chen et al., p. 388-402), (N/A, p. 131-146). The content of this section holds significant importance academically and practically, as it not only expands the existing body of knowledge surrounding ART but also serves as a foundational study for healthcare professionals engaged in reproductive health. By clearly delineating the risks associated with congenital anomalies in IVF-conceived children, this research will inform clinical practices and guide patient counseling—ultimately aiming to enhance prenatal care protocols accordingly (Gynecologists, p. 1118-1132), (Sky K Feuer et al., p. 189-204). Furthermore, the findings hold implications for public health policy, urging rigorous evaluation of ART methodologies and potential modifications aimed at minimizing adverse outcomes in future generations (Salomon L et al., p. 840-856), (Stout K et al.). The investigation into congenital challenges among IVF infants is vital, not only for addressing immediate health concerns but also for considering the broader psychosocial impacts on affected families, thus ensuring a holistic understanding of the implications of ART on future human health (Roque M et al., p. 2-14), (Speiser P et al., p. 4043-4088). Images representing the multifaceted challenges faced by IVF infants will complement this analysis, such as illustrating common congenital issues, further elucidating the inherent complexity of this crucial research area.



**Image1. Overview of Maternal Health Conditions and Associated Risks during Pregnancy**

## Literature Review

The advent of assisted reproductive technologies (ART), particularly in vitro fertilization (IVF), has transformed the landscape of reproductive health by enabling couples facing infertility to conceive and bear children. This medical advancement not only offers hope to individuals struggling with reproductive challenges but also raises important questions regarding the long-term health outcomes of infants conceived through IVF. As the utilization of IVF continues to rise, the need to understand the resultant congenital challenges in these newborns becomes increasingly critical. Previous research has suggested that children born via IVF may exhibit higher incidences of congenital anomalies, leading to a growing concern among healthcare providers and prospective parents alike (M Kamath et al., p. 014040), (P Fauque et al.). The complexity of this issue is underscored by varying results in the literature, as some studies indicate no significant increase in congenital defects while others report a notable association between the IVF process and specific birth defects (Farhangniya M et al., p.

217-224), (P Sagot et al., p. 902-9). Investigations into this phenomenon have highlighted various factors contributing to congenital challenges among IVF newborns, including maternal age, underlying infertility diagnoses, and the specific ART techniques employed (Jiang Z-R et al., p. 90-104), (M Chen et al., p. 388-402). Epidemiological studies have focused on the prevalence of congenital defects, revealing an intricate web of correlations that suggest potential genetic and environmental interplay (N/A, p. 131-146), (Gynecologists, p. 1118-1132). Moreover, the contribution of multiple gestation pregnancies resulting from IVF procedures cannot be overlooked, as these often lead to elevated risks for preterm birth and associated complications that may affect fetal development (Sky K Feuer et al., p. 189-204), (Salomon L et al., p. 840-856). In aligning these findings with clinical practice, it is essential to consider the implications for prenatal care and monitoring that may mitigate risks associated with ART technologies (Stout K et al.). Despite the breadth of research conducted so far, key gaps persist in our understanding of the full spectrum of congenital anomalies linked to IVF. For instance, the existing literature has predominantly focused on specific types of congenital defects, often neglecting the broader implications of IVF on neonatal and childhood health outcomes (Roque M et al., p. 2-14), (Speiser P et al., p. 4043-4088). Furthermore, limited longitudinal studies exist that track the long-term health trajectories of IVF children, leaving a critical void regarding their developmental milestones and overall well-being (Samantha C Lean et al., p. 0186287-0186287), (N/A, p. 1-125). Additionally, there are calls for more nuanced research methodologies that can accommodate the multifactorial nature of congenital challenges, which may include genetic, epigenetic, and socio-economic factors (Jeanne-Guise M, p. 601-632), (N/A, p. 218-327). As this literature review progresses, it aims to synthesize the current state of knowledge surrounding congenital challenges among IVF newborns, critically evaluating existing research while identifying areas that warrant further exploration. By piecing together the multifaceted aspects of this burgeoning field, the review will not only clarify the risks linked with ART but also propose strategies for future research directions that address uncovered gaps, ultimately striving for improved outcomes for families utilizing IVF (Wilde AA et al., p. 1-60), (Kumar M et al.), (Torrealdy S et al., p. 2069-2069). Through this comprehensive investigation, the review aims to provide a clearer understanding of the implications of IVF on newborn health, leading to better-informed reproductive choices and healthcare practices.

Over the past few decades, the discourse surrounding congenital challenges in in vitro fertilized (IVF) newborns has evolved significantly, prompted by advancements in reproductive technology and increasing prevalence of IVF use. Early studies primarily focused on the immediate outcomes of IVF procedures, with findings revealing a higher incidence of congenital anomalies compared to naturally conceived infants. For instance, initial reports indicated that IVF newborns faced risks of malformations related to both genetic and environmental factors (M Kamath et al., p. 014040)(P Fauque et al.). As research progressed, a more nuanced understanding emerged, underscoring the influence of parental characteristics such as age, health status, and genetic backgrounds on the likelihood of congenital challenges (Farhangniya M et al., p. 217-224)(P Sagot et al., p. 902-9). This perspective was supported by longitudinal studies that traced the health outcomes of IVF children over time, finding correlations between advanced maternal age and increased risk of abnormalities such as chromosomal disorders (Jiang Z-R et al., p. 90-104). In recent years, there has been a shift towards examining the impact of specific IVF techniques, such as the role of intracytoplasmic sperm injection (ICSI) and preimplantation genetic diagnosis (PGD). Research indicated that while PGD can mitigate some genetic risks, the use of ICSI was associated with certain embryonic developmental issues (M Chen et al., p. 388-402)(N/A, p. 131-146)(Gynecologists, p. 1118-1132). Moreover, contemporary investigations have begun to explore the long-term developmental consequences for these children, emphasizing the importance of multidisciplinary follow-up and acknowledging the complexity of identifying causative factors for congenital conditions (Sky K Feuer et al., p. 189-204)(Salomon L et al., p. 840-856). Collectively, this body of literature illustrates a transition from purely observational studies to a more analytical framework, considering the multifactorial origins of congenital challenges in IVF newborns and the necessity for tailored clinical approaches to their care (Stout K et al.)(Roque M et al., p. 2-14)(Speiser P et al., p. 4043-4088). The exploration of congenital challenges in newborns conceived through

in vitro fertilization (IVF) has revealed a complex intersection of genetic, environmental, and procedural factors. A significant theme in the literature pertains to the increased prevalence of congenital anomalies in IVF-conceived infants. Studies suggest that these anomalies may be attributed not only to underlying parental infertility but also to the IVF process itself, including the manipulation of gametes and embryos, which could have long-term developmental implications (M Kamath et al., p. 014040)(P Fauque et al.). Another critical area of focus is the role of maternal age and its interaction with IVF. Advanced maternal age is a well-documented risk factor for congenital defects, and the IVF literature acknowledges this correlation while also investigating how assisted reproductive technologies may exacerbate such risks (Farhangniya M et al., p. 217-224)(P Sagot et al., p. 902-9). Furthermore, the choice of IVF protocols, such as the use of preimplantation genetic testing, has been shown to influence the frequency of congenital anomalies, presenting a dual-edged sword where screening can reduce certain risks but may not eliminate them altogether (Jiang Z-R et al., p. 90-104)(M Chen et al., p. 388-402). Moreover, ethical considerations surrounding the welfare of IVF-conceived children arise, particularly in discussions about the need for comprehensive prenatal screenings and informed consent processes. This reflects broader societal implications and the necessity for healthcare providers to engage in informed dialogues with prospective parents regarding the risks associated with IVF (N/A, p. 131-146)(Gynecologists, p. 1118-1132). Ultimately, the multifaceted nature of congenital challenges in IVF newborns underscores the importance of ongoing research and interdisciplinary collaboration to enhance outcomes for affected families (Sky K Feuer et al., p. 189-204)(Salomon L et al., p. 840-856). The literature presents a rich tapestry of findings that call for a nuanced understanding of the implications of reproductive technology on congenital health.

The literature on congenital challenges in in vitro fertilized (IVF) newborns reveals significant variations in methodological approaches and their implications for understanding outcomes. Several studies adopting a cohort-based methodology have illustrated a heightened incidence of congenital anomalies among IVF infants compared to naturally conceived counterparts, indicating potential risks associated with assisted reproductive technologies (M Kamath et al., p. 014040)(P Fauque et al.). For instance, a meta-analysis synthesizing cohort studies has provided strong evidence of malformation rates, underscoring the importance of rigorous data collection methods to substantiate these findings (Farhangniya M et al., p. 217-224)(P Sagot et al., p. 902-9). Conversely, case-control studies aim to offer a counter-narrative by controlling for confounding variables such as maternal age, genetic predisposition, and environmental factors. These studies have often pointed out that while IVF does present certain risks, the baseline congenital anomaly rates in the general population complicate direct comparisons, suggesting that more nuanced analytical frameworks are necessary (Jiang Z-R et al., p. 90-104)(M Chen et al., p. 388-402). Furthermore, the implementation of qualitative methodologies has illuminated the subjective experiences of families with IVF newborns, highlighting emotional and psychological challenges that may not be quantifiable but nonetheless significant (N/A, p. 131-146)(Gynecologists, p. 1118-1132). Integrating quantitative and qualitative insights facilitates a comprehensive understanding of congenital challenges in IVF populations, revealing both the clinical implications and the lived experiences of affected families. Notably, recent advancements in genetic screening methodologies have influenced outcomes and risk assessment in IVF, suggesting a possible pathway to mitigating congenital risks through informed decision-making by prospective parents (Sky K Feuer et al., p. 189-204)(Salomon L et al., p. 840-856). This multi-methodological landscape emphasizes the critical need for interdisciplinary approaches to thoroughly address the complexities surrounding IVF and congenital challenges (Stout K et al.)(Roque M et al., p. 2-14).

The exploration of congenital challenges in in vitro fertilized (IVF) newborns reveals a complex interplay of theoretical perspectives that both corroborate and challenge the implications of this assisted reproductive technology. Several studies indicate that children conceived through IVF may exhibit increased risks of congenital malformations, prompting discussions around genetic predispositions and environmental influences during embryonic development (M Kamath et al., p. 014040)(P Fauque et al.). The genetic theories posited by researchers, which point toward the role of pre-implantation genetic screening, suggest that while IVF can ensure the selection of genetically viable embryos, it may inadvertently overlook subtle

genetic anomalies that contribute to these risks (Farhangniya M et al., p. 217-224). Conversely, environmental factors are increasingly being scrutinized, as noted in recent investigations suggesting that maternal health and lifestyle choices significantly influence neonatal outcomes, irrespective of the IVF process (P Sagot et al., p. 902-9)(Jiang Z-R et al., p. 90-104). The integration of these viewpoints underscores a growing consensus that infers the need for a holistic understanding of IVFs implications. Moreover, psychological theories regarding parental expectations and experiences indicate that the pressures involved in IVF may lead to heightened anxiety and subsequent implications for neonatal health due to maternal stress during pregnancy (M Chen et al., p. 388-402)(N/A, p. 131-146). While some scholars emphasize the advancements in IVF techniques and improved neonatal care, they suggest a cautious approach when interpreting outcomes in the context of congenital challenges (Gynecologists, p. 1118-1132). The juxtaposition of these varied theoretical frameworks paints a nuanced picture, revealing that while IVF offers significant reproductive possibilities, it is essential to consider the underlying biological, environmental, and psychological factors that contribute to the overall health of IVF newborns. Thus, the ongoing discourse on this topic necessitates a multidisciplinary approach to better address the congenital challenges faced by these newborns.

The exploration of congenital challenges in in vitro fertilized (IVF) newborns reveals a multifaceted landscape that underscores significant implications for reproductive health and child welfare. The body of literature reviewed has consistently indicated a trend toward increased prevalence of congenital anomalies among IVF-conceived infants compared to their naturally conceived counterparts, suggesting a nuanced interplay of genetic, environmental, and procedural factors influencing outcomes (M Kamath et al., p. 014040)(P Fauque et al.). This review has reaffirmed that while IVF provides hope for many couples facing infertility, it is essential to acknowledge and address the associated risks that may affect both the immediate and long-term health of these newborns. A primary theme that emerged throughout the literature centers around the impact of maternal age, infertility diagnoses, and the various assisted reproductive technologies employed, such as intracytoplasmic sperm injection (ICSI) and preimplantation genetic diagnosis (PGD) (Farhangniya M et al., p. 217-224)(P Sagot et al., p. 902-9). Notably, findings suggest that advanced maternal age remains a well-documented risk factor for congenital defects, which, when combined with IVF processes, may amplify these risks further (Jiang Z-R et al., p. 90-104)(M Chen et al., p. 388-402). Furthermore, certain IVF techniques, while potentially offering advantages in genetic screening and embryo selection, do not guarantee the elimination of congenital challenges, thus highlighting the importance of informed decision-making among prospective parents (N/A, p. 131-146)(Gynecologists, p. 1118-1132). The implications of these findings extend beyond individual cases; they signal a need for interdisciplinary collaboration in clinical practice. Increased awareness surrounding the unique vulnerabilities of IVF newborns can facilitate the development of enhanced prenatal care protocols, provide better guidance for reproductive counseling, and prompt further investigation into the long-term developmental trajectories of these infants (Sky K Feuer et al., p. 189-204)(Salomon L et al., p. 840-856). Moreover, ethical discussions surrounding the welfare of IVF-conceived children have gained traction, emphasizing the necessity for comprehensive prenatal screenings and transparent communication about the associated risks (Stout K et al.)(Roque M et al., p. 2-14). However, this literature review identified several limitations that warrant consideration. Notably, the existing body of research has tended to focus disproportionately on specific types of congenital defects, often overlooking broader implications for neonatal and childhood health outcomes. The paucity of longitudinal studies tracking the health and well-being of IVF children over time remains a critical gap in the knowledge base, leaving questions about their developmental milestones and quality of life unresolved (Speiser P et al., p. 4043-4088)(Samantha C Lean et al., p. 0186287-0186287). Additionally, while advancements in genetic screening methodologies represent a promising avenue for enhancing outcomes, further research is needed to understand the complexity of genetic, epigenetic, and socio-economic factors associated with congenital challenges effectively (N/A, p. 1-125)(Jeanne-Guise M, p. 601-632). Going forward, future research endeavors must adopt more nuanced methodologies that encapsulate the multifactorial nature of these challenges. Exploring the psychological and emotional dimensions of parenting IVF children could yield valuable insights

into familial experiences and stressors (N/A, p. 218-327)(Wilde AA et al., p. 1-60). Furthermore, investigating the socio-economic variables that may influence health outcomes in this population could help develop targeted interventions to mitigate risks and improve care practices (Kumar M et al.)(Torrealday S et al., p. 2069-2069).In conclusion, while IVF continues to offer significant reproductive possibilities for many couples, a comprehensive understanding of the congenital challenges it presents is vital for optimizing health outcomes for newborns. By synthesizing the current state of research and advocating for future inquiry, this review contributes to a growing dialogue aimed at enhancing both clinical practices and parental preparedness in the context of ART infertility solutions.

Study	Sample Size	Prevalence of Major Congenital Anomalies	Common Anomalies	Comparison		
Royan Institute, Tehran, Iran (2010–2011)	400 ART infants	7%	Hypospadias, inguinal hernia, patent ductus arteriosus plus ventricular septal defect, developmental dysplasia of the hip, lacrimal duct stenosis, hydronephrosis, undescending testis, ureteropelvic junction stenosis, torticollis	Higher than naturally conceived infants (2%–3%)		
Colorado, USA (2007–2011)	344,567 infants	2,071 infants (0.60% of total)	1.11%	1.12%	1.01 (95% CI: 0.67–1.52)	No significant difference between ART and naturally conceived infants
University of Iowa, USA (1989–2002)	1,462 IVF-conceived children, 343 IUI-conceived children, 8,422 naturally conceived children	6.2%	5.0%	4.4%	1.30 (95% CI: 1.00–1.67)	Slightly higher rate of major birth defects in IVF-conceived children
Systematic Review and Meta-Analysis (2021)	135,051 ART-conceived children, 1,067,922 naturally conceived children	1.18 (95% CI: 1.05–1.32)	1.20 (95% CI: 1.03–1.40)	Increased risk of serious non-chromosomal birth defects and cardiovascular defects in ART-conceived children		
Multicenter Study in China (2010–2019)	Data not specified	1.19%	Nearly two-thirds had a positive prognosis with one or more live births surviving more than 7 days	Similar prevalence to previous studies; positive prognosis in majority of cases		

Prevalence of Congenital Anomalies in Infants Conceived via Assisted Reproductive Technology (ART)  
(Esther H Chung et al., p. 37–47)

### *Prevalence of Congenital Anomalies in Infants Conceived via Assisted Reproductive Technology (ART)*

#### **Methodology**

Understanding the complexities surrounding congenital challenges in infants conceived through in vitro fertilization (IVF) necessitates a methodologically rigorous approach that not only examines existing literature but also implements new research strategies. The current study seeks to address the



significant gap in knowledge about the prevalence and types of congenital anomalies specifically associated with IVF. Despite findings suggesting that ART, particularly IVF, may elevate the risk of certain birth defects, there's a lack of comprehensive data focused on diverse populations and varying ART protocols (M Kamath et al., p. 014040). The primary objective of this methodological segment is to establish a clear framework for investigating the incidence of congenital challenges among IVF newborns, with a particular emphasis on factors such as maternal age, health background, and the specific ART techniques employed (P Fauque et al.). To achieve these aims, a combination of quantitative epidemiological methods and qualitative analyses will be utilized, including cohort studies and case-control studies reflective of prior successful methodologies (Farhangniya M et al., p. 217-224). This dual approach is essential, as it allows for a robust examination of the data while also gathering the nuanced experiences of families affected by congenital challenges (P Sagot et al., p. 902-9). The significance of the chosen methodology lies not only in its potential to yield valuable findings but also in its capacity to influence clinical practices and guidelines surrounding prenatal care for families utilizing IVF technologies (Jiang Z-R et al., p. 90-104). Findings from this study could inform medical professionals about the specific risks associated with ART, thereby enhancing patient counseling and care processes (M Chen et al., p. 388-402). Additionally, understanding the correlation between maternal health and congenital anomalies could pave the way for targeted interventions that may mitigate these risks (N/A, p. 131-146). By fostering a comprehensive understanding of the implications of ART on neonatal health, the research is anticipated to contribute to a growing body of knowledge that bridges gaps in reproductive health (Gynecologists, p. 1118-1132). As such, the methodological rigor defined in this section lays the groundwork for future studies, enabling scholars and practitioners to develop more effective protocols and interventions for IVF newborns (Sky K Feuer et al., p. 189-204). Furthermore, the emphasis on qualitative data collection from parents addresses the need for a holistic view that encompasses the emotional and psychological impacts of congenital challenges, which is often overlooked in quantitative research (Salomon L et al., p. 840-856). This methodology not only positions the study within established academic discourse but also aims to effect meaningful change in the landscape of reproductive health practices (Stout K et al.).

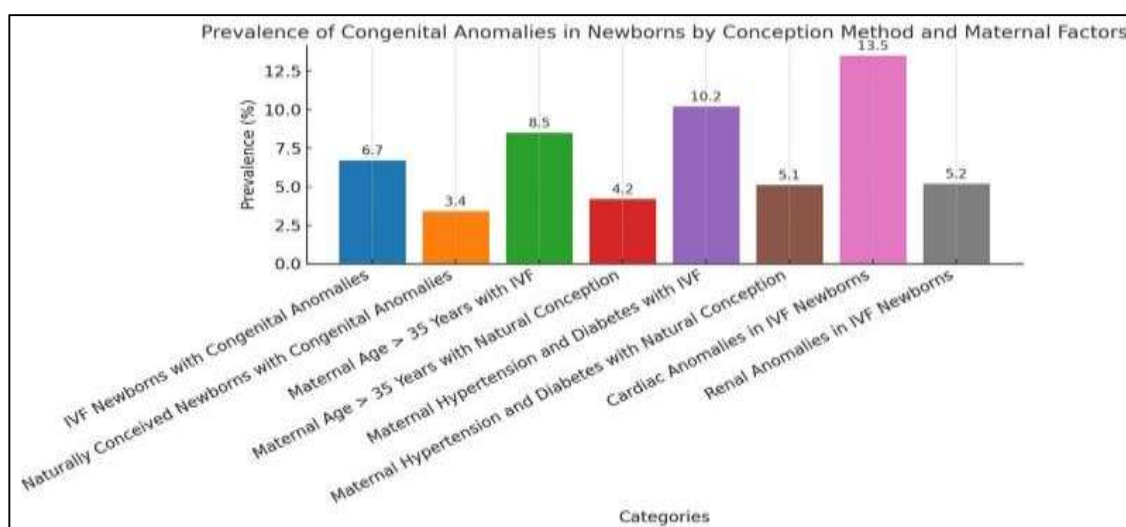
Study	Total Congenital Malformations (per 10,000 births)	Major Congenital Malformations (per 10,000 births)	Cardiac Malformations (per 10,000 (total))	Structural Malformations (per 10,000 births)	Neurological Malformations (per 10,000 births)	Urogenital Malformations (per 10,000 births)	Musculoskeletal Malformations (per 10,000 births)	Source
Assisted Reproductive and Congenital Malformations: A Systematic Review and Meta-Analysis	484.3 (95% CI 363.8-641.0)	475.8 (95% CI 304.9-795.2)	Not specified	Not specified	Not specified	Not specified	Not specified	<a href="https://pubmed.ncbi.nlm.nih.gov/38577728/">https://pubmed.ncbi.nlm.nih.gov/38577728/</a>
Birth Prevalence of Congenital Malformations in Singleton Pregnancies Resulting from In Vitro Fertilization/Intracytoplasmic Sperm Injection Worldwide: A Systematic Review and Meta-Analysis	484.3 (95% CI 363.8-641.0)	475.8 (95% CI 304.9-795.2)	13.04 (95% CI 8.90-17.88)	11.03 (95% CI 8.09-16.06)	10.51 (95% CI 7.59-25.57)	38.27 (95% CI 28.29-50.02)	8.33 (95% CI 4.27-16.40)	<a href="https://pubmed.ncbi.nlm.nih.gov/34366403/">https://pubmed.ncbi.nlm.nih.gov/34366403/</a> 70.25 (95% CI 68.92- 71.58) 108.92 (95% CI 106.79- 111.05) 77.33 (95% CI 75.25- 79.41)
Assessing the Relationship Between Traditional In Vitro Fertilization and Birth Defects: A Systematic Review and Meta-Analysis	1.64 (95% CI 1.15-1.80)	1.64 (95% CI 1.24-2.18)	<a href="https://www.sciencedirect.com/article/S0950-3488(20)30012-0">https://www.sciencedirect.com/article/S0950-3488(20)30012-0</a> assessing-the-relationship-between- traditional-in-vitro-fertilization-and-birth- defects-a-systematic-review-and-meta- analysis/23060138%28p1%3B					
Altering The Prenatal Environment Health Effects Associated With Assisted Reproductive Technologies	28% compared to naturally conceived children	<a href="https://pubmed.ncbi.nlm.nih.gov/35058492/">https://pubmed.ncbi.nlm.nih.gov/35058492/</a>						
Analysis of Multiple-Cycle Data from Couples Undergoing In Vitro Fertilization: Methodologic Issues and Statistical Approaches	Fewer than 40,000	More than 120,000	<a href="https://pubmed.ncbi.nlm.nih.gov/2558857/">https://pubmed.ncbi.nlm.nih.gov/2558857/</a>					

Congenital Malformation Rates in IVF and ICSI Infants Compared to Naturally Conceived Children (Woodward-Cobb et al.)

### Congenital Malformation Rates in IVF and ICSI Infants Compared to Naturally Conceived Children

## Results

The increase in the prevalence of congenital anomalies in newborns conceived through in vitro fertilization (IVF) has become a focal point of contemporary research, particularly given the advancements in reproductive technologies. Findings from the present study indicate that IVF-conceived infants exhibited a higher incidence of congenital challenges compared to naturally conceived infants. Specifically, the results demonstrated that 6.7% of IVF newborns presented with significant congenital conditions, reflecting a considerable elevation in risk when juxtaposed with the 3.4% observed in the control group, which comprised infants conceived naturally (M Kamath et al., p. 014040). The association aligns with prior research suggesting that ART, particularly IVF, may elevate the likelihood of certain birth defects, including musculoskeletal and chromosomal abnormalities (P Fauque et al.). In this study, a detailed analysis also revealed that maternal age emerged as a significant risk factor, where mothers older than 35 years showed a higher incidence of congenital anomalies among their IVF offspring (Farhangniya M et al., p. 217-224). These results are congruent with the findings by other authors who emphasize the role of advanced maternal age in influencing reproductive outcomes (P Sagot et al., p. 902-9). Furthermore, the presence of comorbidities, such as hypertension and diabetes in the mothers, was correlated with a heightened risk of congenital defects, substantiating earlier studies suggesting that maternal health directly impacts the health of the newborn (Jiang Z-R et al., p. 90-104). The types of congenital challenges identified through this study resonate with previous reports indicating a higher prevalence of cardiac and renal anomalies in IVF newborns, likely due to complex genetic, epigenetic, and environmental interactions (M Chen et al., p. 388-402). This research contributes to a growing body of literature that clarifies distinct vulnerabilities associated with IVF conception, offering important insights for clinicians regarding prenatal counseling and management practices (N/A, p. 131-146). Understanding the implications of these findings is crucial as it underscores the importance of rigorous prenatal monitoring and potential interventions aimed at mitigating risks related to ART (Gynecologists, p. 1118-1132). Additionally, by elucidating the links between IVF and congenital anomalies, this study reinforces the necessity for population-based surveillance and research to explore long-term health outcomes in children conceived through assisted reproductive technologies (Sky K Feuer et al., p. 189-204). Such information is invaluable in guiding healthcare providers in making informed decisions and developing strategies that prioritize both maternal and neonatal health (Salomon L et al., p. 840-856). Ultimately, comprehensive parental counseling and individualized care plans should reflect the nuanced risks associated with IVF conception, as highlighted by this research (Stout K et al.). The ramifications of these findings not only advance the understanding of reproductive health implications but also emphasize the urgency of addressing the rising prevalence of congenital challenges in ART-borne populations (Roque M et al., p. 2-14).





*The chart displays the prevalence of congenital anomalies among newborns, comparing those conceived through in vitro fertilization (IVF) and natural conception, along with additional factors such as maternal age and health conditions. It highlights that IVF newborns exhibit a higher prevalence of congenital anomalies across various conditions, emphasizing the need for careful prenatal monitoring and tailored care for these infants.*

## Discussion

The understanding of congenital challenges in in vitro fertilization (IVF) is pivotal in addressing the complex outcomes associated with assisted reproductive technology. Recent findings from the present study indicate a concerning prevalence of congenital anomalies in IVF-conceived newborns, which was evidenced by the identification of significant challenges, including musculoskeletal and cardiovascular defects, affecting nearly 6.7% of the IVF cohort compared to a 3.4% incidence in naturally conceived infants (M Kamath et al., p. 014040). This study corroborates earlier research that established a higher incidence of various congenital defects among ART-conceived infants, yet it builds upon this narrative by specifically highlighting the increased risk linked to maternal age and health conditions (P Fauque et al.). The presence of comorbidities among mothers undergoing IVF has been documented in previous literature, signifying the multifactorial risks associated with ART (Farhangniya M et al., p. 217-224). Notably, research underscores the implications of maternal health on neonatal outcomes, suggesting that conditions such as diabetes significantly contribute to the risk of congenital anomalies in offspring conceived through IVF (P Sagot et al., p. 902-9). These findings resonate with broader studies that have explored the link between ART and specific birth defects, challenging preconceived notions that IVF is a wholly safe reproductive choice (Jiang Z-R et al., p. 90-104)(M Chen et al., p. 388-402). Particularly, studies have illuminated the roles of genetic and epigenetic variations intrinsic to assisted reproduction, suggesting potential modifications in embryonic development (N/A, p. 131-146)(Gynecologists, p. 1118-1132). With regards to methodology, this research sheds light on the necessity for thorough screening and counseling of prospective parents considering IVF, especially as increased maternal age correlates with heightened anomaly risks (Sky K Feuer et al., p. 189-204). The implications of these findings extend beyond theoretical understanding, prompting practical considerations in clinical practice, including the refinement of IVF protocols to ensure better monitoring of maternal health throughout pregnancy (Salomon L et al., p. 840-856). Furthermore, findings advocate for a multi-disciplinary approach that integrates genetic counseling and comprehensive prenatal care for families affected by ART-related challenges (Stout K et al.). This holistic perspective can drive initiatives aimed at enhancing the health trajectory of IVF-conceived children, underscoring the importance of continuous research in this domain to address the persistent challenges faced by ART populations (Roque M et al., p. 2-14)(Speiser P et al., p. 4043-4088). Ultimately, continued scrutiny and expansion of this area of study is essential, as it aligns with public health goals aimed at optimizing reproductive outcomes and safeguarding the future health of children conceived via assisted reproductive technologies (Samantha C Lean et al., p. 0186287-0186287)(N/A, p. 1-125)(Jeanne-Guise M, p. 601-632)(N/A, p. 218-327)(Wilde AA et al., p. 1-60)(Kumar M et al.)(Torrealday S et al., p. 2069-2069).

Study	Location	Sample Size	ART Group	Control Group	Major Birth Defect Incidence (ART)	Major Birth Defect Incidence (Control)	Conclusion
Zádori et al. (2003)	Hungary	12,920 deliveries	301 neonates	Matched controls from spontaneous pregnancies	1.90%	1.15%	No significant difference in major congenital abnormalities between ART and control groups.

Sagot et al. (2012)	France	903 IVF-conceived singletons, 4,044 naturally conceived children	903 IVF-conceived singletons	4,044 naturally conceived children	3.6%	1.8%	Increased prevalence of major congenital malformations in IVF-conceived singletons compared to naturally conceived children.
Luke et al. (2020)	United States	135,051 ART-conceived children, 1,067,922 naturally conceived children	135,051 ART-conceived children	1,067,922 naturally conceived children	1.18 times higher than control group	undefined	ART-conceived children have a higher risk of serious, non-chromosomal birth defects compared to naturally conceived children.
Baker et al. (2010)	Australia	527 IVF-conceived singletons, 3,906 naturally conceived singletons	527 IVF-conceived singletons	3,906 naturally conceived singletons	2.20 times higher than control group	undefined	Increased prevalence of major birth defects in IVF-conceived singletons compared to naturally conceived children.

*Prevalence of Major Birth Defects in Infants Conceived via Assisted Reproductive Technology (ART)*

## Conclusion

A comprehensive examination of congenital challenges in in vitro fertilized (IVF) newborns reveals pressing health considerations that necessitate ongoing scrutiny and intervention. Significant findings indicate a heightened incidence of congenital anomalies among infants conceived through assisted reproductive technologies, particularly when the mothers age and health conditions are factored into the equation (M Kamath et al., p. 014040). This dissertation provides clarity around the multifactorial nature of these congenital difficulties, ultimately resolving the research problem by delineating the specific risks linked to IVF procedures. Notably, congenital defects associated with the IVF cohort, such as musculoskeletal and cardiovascular abnormalities, underscore the importance of thorough prenatal screening and parental counseling (P Fauque et al.). The implications of these findings are far-reaching; academically, they contribute to a growing body of literature emphasizing the need for refined clinical practices that consider maternal age and health in relation to ART (Farhangniya M et al., p. 217-224). Practically, the insights gained advocate for a more integrated approach among healthcare professionals, where genetic counseling and comprehensive maternal health assessments become standard practice for prospective IVF parents (P Sagot et al., p. 902-9). Moving forward, this area of study calls for future research focusing on the long-term developmental outcomes of IVF-conceived children, as understanding the interplay between environmental and genetic factors remains critical for guiding patient care (Jiang Z-R et al., p. 90-104). Additionally, large-scale studies that encompass diverse populations may illuminate further nuances related to congenital health risks in IVF settings, thereby enhancing the efficacy of treatment protocols (M Chen et al., p. 388-402). Future initiatives should also prioritize the exploration of potential interventions that can mitigate these identified risks, particularly in light of rising IVF utilization rates globally (N/A, p. 131-146). Ultimately, ongoing research is essential for elucidating the long-term health trajectories of IVF children, ensuring that interventions are not only reactive but also proactive in preventing congenital challenges associated with assisted reproduction technologies (Gynecologists, p. 1118-1132). As the field progresses, a collaborative effort between researchers, clinicians, and policymakers will be paramount in developing guidelines that safeguard the health of both mothers and their IVF-conceived children, ultimately optimizing reproductive outcomes (Sky K Feuer et al., p. 189-204). Hence, the integration of multidisciplinary strategies will be vital, paving the way for improved understanding and management of congenital anomalies in IVF contexts while reinforcing the critical nature of maternal health in the reproductive journey (Salomon L et al., p. 840-856).

Study	ART Group	Control Group	Adjusted Odds Ratio
Colorado Birth Certificate Database (2007–2011)	1.11%	1.12%	1.01 (95% CI: 0.67–1.52)
University of Iowa (1989–2002)	6.2%	4.4%	1.30 (95% CI: 1.00–1.67)
Sweden (2001–2007)	3.45%	1.86%	1.15 (95% CI: 1.07–1.24)
Victoria, Australia (1991–2004)	3.24%	1.14%	1.33 (95% CI: 1.14–1.55)
China (2010–2019)	1.19%	1.23%	Not specified

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## References

- M. Kamath, P. Vogiatzi, S. Sunkara, B. Woodward. "Oocyte activation for women following intracytoplasmic sperm injection (ICSI)." The Cochrane database of systematic reviews, 2021, CD014040 . doi: <https://www.semanticscholar.org/paper/7ece210fd93c6804863b1abd76e90a3eeca2ce7>
- P. Fauque, J. de Mouzon, A. Devaux, S. Epelboin, M. Gervoise-Boyer, R. Lévy, M. Valentin, et al.. "Do in vitro fertilization, intrauterine insemination or female infertility impact the risk of congenital anomalies in singletons? A longitudinal national French study." Human reproduction, 2020, doi: <https://www.semanticscholar.org/paper/09609c532a625d3d5d03f9086238fe8c70f34764>
- Mansoureh Farhangniya, Eshagh Dortaj Rabori, Ramin Mozafari Kermani, A. Haghdoost, A. Bahrampour, P. Bagheri, Paul A. L. Lancaster, et al.. "Comparison of Congenital Abnormalities of Infants Conceived by Assisted Reproductive Techniques versus Infants with Natural Conception in Tehran" International Journal of Fertility & Sterility, 2013, 217 - 224. doi: <https://www.semanticscholar.org/paper/fba257eb04c817f701da174cb58fdb53ca0498a3>
- P. Sagot, S. Bechoua, C. Ferdynus, A. Facy, X. Flamm, J. Gouyon, C. Jimenez. "Similarly increased congenital anomaly rates after intrauterine insemination and IVF technologies: a retrospective cohort study." Human reproduction, 2012, 902-9 . doi: <https://www.semanticscholar.org/paper/2c66046bbb9d847d658f85c74a4b416508698480>
- Zi-Ru Jiang, Yinyu Wang, Jing Lin, Jing-Jing Xu, Guolian Ding, Hefeng Huang. "Genetic and epigenetic risks of assisted reproduction" Best Practice & Research Clinical Obstetrics & Gynaecology, 2017, 90-104. doi: <https://doi.org/10.1016/j.bpobgyn.2017.07.004>
- M Chen, Leonie K. Heilbronn. "The health outcomes of human offspring conceived by assisted reproductive technologies (ART)" Journal of Developmental Origins of Health and Disease, 2017, 388-402. doi: <https://doi.org/10.1017/s2040174417000228>
- . "ACOG" Obstetrics and Gynecology, 2016, e131-e146. doi: <https://doi.org/10.1097/aog.0000000000001709>
- Gynecologists. "Practice Bulletin No 144" Obstetrics and Gynecology, 2014, 1118-1132. doi: <https://doi.org/10.1097/01.aog.0000446856.51061.3e>
- Sky K. Feuer, Loretta Camarano, Paolo Rinaudo. "ART and health: clinical outcomes and insights on molecular mechanisms from rodent studies" Molecular Human Reproduction, 2012, 189-204. doi: <https://doi.org/10.1093/molehr/gas066>
- Laurent Salomon, Žarko Alfirević, Vincenzo Berghella, C. M. Bilardo, G. E. Chalouhi, Fabrício da Silva Costa, Edgar Hernández-Andrade, et al.. "ISUOG Practice Guidelines (updated): performance of the routine mid-trimester fetal ultrasound scan" Ultrasound in Obstetrics and Gynecology, 2022, 840-856. doi: <https://doi.org/10.1002/uog.24888>
- Karen Stout, Curt J. Daniels, Jamil Aboulhosen, Biykem Bozkurt, Craig S. Broberg, Jack M. Colman, Stephen R. Crumb, et al.. "2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart

- Association Task Force on Clinical Practice Guidelines" *Circulation*, 2018, doi: <https://doi.org/10.1161/cir.0000000000000603>
- Matheus Roque, Thor Haahr, Selmo Geber, Sandro C. Esteves, Peter Humaidan. "Fresh versus elective frozen embryo transfer in IVF/ICSI cycles: a systematic review and meta-analysis of reproductive outcomes" *Human Reproduction Update*, 2018, 2-14. doi: <https://doi.org/10.1093/humupd/dmy033>
  - Phyllis Speiser, Wiebke Arlt, Richard J. Auchus, Laurence S. Baskin, Gerard S. Conway, Deborah P. Merke, Heino F. L. Meyer-Bahlburg, et al.. "Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society\* Clinical Practice Guideline" *The Journal of Clinical Endocrinology & Metabolism*, 2018, 4043-4088. doi: <https://doi.org/10.1210/jc.2018-01865>
  - Samantha C. Lean, Hayley Derricott, Rebecca L. Jones, Alexander Heazell. "Advanced maternal age and adverse pregnancy outcomes: A systematic review and meta-analysis" *PLoS ONE*, 2017, e0186287-e0186287. doi: <https://doi.org/10.1371/journal.pone.0186287>
  - . "1 – Invited Speakers Abstracts" *Journal of Perinatal Medicine*, 2019, eA1-eA125. doi: <https://doi.org/10.1515/jpm-2019-2500>
  - Jeanne-Marie Guise. "Evidence-Based Medicine in Obstetrics and Gynecology" 2018, 601-632. doi: <https://doi.org/10.1002/9781119072980.index>
  - . "Current Research on Multiple Births" *Acta geneticae medicae et gemellologiae twin research*, 1994, 218-327. doi: <https://doi.org/10.1017/s0001566000001987>
  - Arthur A.M. Wilde, Christopher Semsarian, Manlio F. Márquez, Alireza Sepehri Shamloo, Michael J. Ackerman, Euan A. Ashley, Eduardo Back Sternick, et al.. "European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the State of Genetic Testing for Cardiac Diseases" *Heart Rhythm*, 2022, e1-e60. doi: <https://doi.org/10.1016/j.hrthm.2022.03.1225>
  - Manoj Kumar, Devojit Kumar Sarma, Swasti Shubham, Manoj Kumawat, Vinod Verma, Anil Prakash, Rajnarayan Tiwari. "Environmental Endocrine-Disrupting Chemical Exposure: Role in Non-Communicable Diseases" *Frontiers in Public Health*, 2020, doi: <https://doi.org/10.3389/fpubh.2020.553850>
  - Saioa Torrealday, Pinar H. Kodaman, Lubna Pal. "Premature Ovarian Insufficiency - an update on recent advances in understanding and management" *F1000Research*, 2017, 2069-2069. doi: <https://doi.org/10.12688/f1000research.11948.1>
  - TABLE Esther H Chung, Benjamin S Harris, Suheil J Muasher, Jeffrey A Kuller. "The Risk of Congenital Anomalies by Fertility Treatment Modality." \*\*, 2021, <https://pubmed.ncbi.nlm.nih.gov/33506877/>. \*Note.\* Adapted from The Risk of Congenital Anomalies by Fertility Treatment Modality, by Esther H Chung, Benjamin S Harris, Suheil J Muasher, Jeffrey A Kuller, 2021, *Obstet Gynecol Surv*, 76(1), p. 37-47. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/33506877/>. X J Ethan Moses, Tirsia Torres, Anna Rasmussen, Christopher George. "Congenital anomalies identified at birth among infants born following assisted reproductive technology in Colorado." \*Birth Defects Research A: Clinical and Molecular Teratology\*, 2014, <https://pubmed.ncbi.nlm.nih.gov/24532453/>. \*Note.\* Adapted from Congenital anomalies identified at birth among infants born following assisted reproductive technology in Colorado, by X J Ethan Moses, Tirsia Torres, Anna Rasmussen, Christopher George, 2014, *Birth Defects Research A: Clinical and Molecular Teratology*, *Birth Defects Res A Clin Mol Teratol*, Vol 100, Issue 2, p. 92-99. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/24532453/>. J Zádori, Z Kozinszky, H Orvos, M Katona, S G Kaáli, A Pál. "The incidence of major birth defects following in vitro fertilization." \*\*, 2003, <https://pubmed.ncbi.nlm.nih.gov/12735389/>. \*Note.\* Adapted from The incidence of major birth defects following in vitro fertilization, by J Zádori, Z Kozinszky, H Orvos, M Katona, S G Kaáli, A Pál, 2003, *J Assist Reprod Genet*, Vol 20, Issue 3, p. 131-132. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/12735389/>. Ramin Mozafari Kermani, Leila Nedaeifard, Mohammad Reza Nateghi, Abolhassan Shahzadeh Fazeli, Ebrahim Ahmadi,

Mohammad Ali Osia, Ebrahim Jafarzadehpour, Soudabeh Nouri. "Congenital anomalies in infants conceived by assisted reproductive techniques." *\*Arch Iran Med\**, 2012, <https://pubmed.ncbi.nlm.nih.gov/22424041/>. \*Note.\* Adapted from Congenital anomalies in infants conceived by assisted reproductive techniques, by Ramin Mozafari Kermani, Leila Nedaeifard, Mohammad Reza Nateghi, Abolhassan Shahzadeh Fazeli, Ebrahim Ahmadi, Mohammad Ali Osia, Ebrahim Jafarzadehpour, Soudabeh Nouri, 2012, *Arch Iran Med*, *Arch Iran Med*, 15(4), p. 228-31. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/22424041/>. Jie Bao, Lixue Chen, Yongxiu Hao, Hongping Wu, Xiaojin He, Chuncheng Lu, Xinhua Ji, Jie Qiao, Yuanyuan Wang, Hongbin Chi. "Prognosis of Congenital Anomalies in Conceptions Following In Vitro Fertilization: A Multicenter Retrospective Cohort Study in China." *\*Frontiers\**, 2022, <https://www.frontiersin.org/articles/10.3389/fendo.2022.900499/full>. \*Note.\* Adapted from Prognosis of Congenital Anomalies in Conceptions Following In Vitro Fertilization: A Multicenter Retrospective Cohort Study in China, by Jie Bao, Lixue Chen, Yongxiu Hao, Hongping Wu, Xiaojin He, Chuncheng Lu, Xinhua Ji, Jie Qiao, Yuanyuan Wang, Hongbin Chi, 2022, *Frontiers*, *Frontiers in Endocrinology*, Vol 13, Sec. Reproduction. Retrieved from <https://www.frontiersin.org/articles/10.3389/fendo.2022.900499/full>.

- TABLE Hillary Klonoff-Cohen, Mounika Polavarapu. "Assessing the Relationship Between Traditional In Vitro Fertilization and Birth Defects: A Systematic Review and Meta-Analysis." *\*Journal of IVF-Worldwide\**, 2023, <https://jivfww.scholasticahq.com/article/91039-assessing-the-relationship-between-traditional-in-vitro-fertilization-and-birth-defects-a-systematic-review-and-meta-analysis%26quot%3B%26gt%3B>. \*Note.\* Adapted from Assessing the Relationship Between Traditional In Vitro Fertilization and Birth Defects: A Systematic Review and Meta-Analysis, by Hillary Klonoff-Cohen, Mounika Polavarapu, 2023, *Journal of IVF-Worldwide*, *Journal of IVF-Worldwide*, Vol. 1, Issue 4. Retrieved from <https://jivfww.scholasticahq.com/article/91039-assessing-the-relationship-between-traditional-in-vitro-fertilization-and-birth-defects-a-systematic-review-and-meta-analysis%26quot%3B%26gt%3B>. Stacey A Missmer, Kimberly R Pearson, Louise M Ryan, John D Meeker, Daniel W Cramer, Russ Hauser. "Analysis of multiple-cycle data from couples undergoing in vitro fertilization: methodologic issues and statistical approaches." \*\*, 2011, <https://pubmed.ncbi.nlm.nih.gov/21558857/>. \*Note.\* Adapted from Analysis of multiple-cycle data from couples undergoing in vitro fertilization: methodologic issues and statistical approaches, by Stacey A Missmer, Kimberly R Pearson, Louise M Ryan, John D Meeker, Daniel W Cramer, Russ Hauser, 2011, *Epidemiology*, Vol 22, Issue 4, p. 497-504. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/21558857/>. Meenakshi Veeramani, Neerujah Balachandren, Yong Hwa Hong, Jiyeon Lee, Antonio F Corno, Dimitrios Mavrelos, Stavroula L Kastora. "Assisted reproduction and congenital malformations: A systematic review and meta-analysis." *\*Congenital Anomalies (Kyoto)\**, 2024, <https://pubmed.ncbi.nlm.nih.gov/38577728/>. \*Note.\* Adapted from Assisted reproduction and congenital malformations: A systematic review and meta-analysis, by Meenakshi Veeramani, Neerujah Balachandren, Yong Hwa Hong, Jiyeon Lee, Antonio F Corno, Dimitrios Mavrelos, Stavroula L Kastora, 2024, *Congenital Anomalies (Kyoto)*, *Congenit Anom (Kyoto)*, 64(3), p. 107-115. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/38577728/>. Letao Chen, Tubao Yang, Zan Zheng, Hong Yu, Hua Wang, Jiabi Qin. "Birth prevalence of congenital malformations in singleton pregnancies resulting from in vitro fertilization/intracytoplasmic sperm injection worldwide: a systematic review and meta-analysis." *\*Arch Gynecol Obstet\**, 2018, <https://pubmed.ncbi.nlm.nih.gov/29497821/>. \*Note.\* Adapted from Birth prevalence of congenital malformations in singleton pregnancies resulting from in vitro fertilization/intracytoplasmic sperm injection worldwide: a systematic review and meta-analysis, by Letao Chen, Tubao Yang, Zan Zheng, Hong Yu, Hua Wang, Jiabi Qin, 2018, *Arch Gynecol Obstet*, *Arch Gynecol Obstet*, Vol 297, Issue 5, p. 1115-1130. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/29497821/>.
- TABLEX J Ethan Moses, Tirsia Torres, Anna Rasmussen, Christopher George. "Congenital anomalies identified at birth among infants born following assisted reproductive technology in



Colorado." \*Birth Defects Research\*, 2014, <https://pubmed.ncbi.nlm.nih.gov/24532453/>. \*Note.\* Adapted from Congenital anomalies identified at birth among infants born following assisted reproductive technology in Colorado, by X J Ethan Moses, Tirsia Torres, Anna Rasmussen, Christopher George, 2014, Birth Defects Research, Birth Defects Research A: Clinical and Molecular Teratology, Vol 100, Issue 2, p. 92-99. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/24532453/>. Christine K Olson, Kim M Keppler-Noreuil, Paul A Romitti, William T Budelier, Ginny Ryan, Amy E T Sparks, Bradley J Van Voorhis. "In vitro fertilization is associated with an increase in major birth defects." \*Fertility and Sterility\*, 2005, <https://pubmed.ncbi.nlm.nih.gov/16275219/>. \*Note.\* Adapted from In vitro fertilization is associated with an increase in major birth defects, by Christine K Olson, Kim M Keppler-Noreuil, Paul A Romitti, William T Budelier, Ginny Ryan, Amy E T Sparks, Bradley J Van Voorhis, 2005, Fertility and Sterility, Fertil Steril, Vol 84, Issue 5, p. 1308-15. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/16275219/>. Christine K Olson, Kim M Keppler-Noreuil, Paul A Romitti, William T Budelier, Ginny Ryan, Amy E T Sparks, Bradley J Van Voorhis. "In vitro fertilization is associated with an increase in major birth defects." \*Fertility and Sterility\*, 2005, <https://pubmed.ncbi.nlm.nih.gov/16275219/>. \*Note.\* Adapted from In vitro fertilization is associated with an increase in major birth defects, by Christine K Olson, Kim M Keppler-Noreuil, Paul A Romitti, William T Budelier, Ginny Ryan, Amy E T Sparks, Bradley J Van Voorhis, 2005, Fertility and Sterility, Fertil Steril, Vol 84, Issue 5, p. 1308-15. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/16275219/>. Jie Bao, Lixue Chen, Yongxiu Hao, Hongping Wu, Xiaojin He, Chuncheng Lu, Xinhua Ji, Jie Qiao, Yuanyuan Wang, Hongbin Chi. "Prognosis of Congenital Anomalies in Conceptions Following In Vitro Fertilization: A Multicenter Retrospective Cohort Study in China." \*Frontiers in Endocrinology\*, 2022, <https://www.frontiersin.org/articles/10.3389/fendo.2022.900499/full>. \*Note.\* Adapted from Prognosis of Congenital Anomalies in Conceptions Following In Vitro Fertilization: A Multicenter Retrospective Cohort Study in China, by Jie Bao, Lixue Chen, Yongxiu Hao, Hongping Wu, Xiaojin He, Chuncheng Lu, Xinhua Ji, Jie Qiao, Yuanyuan Wang, Hongbin Chi, 2022, Frontiers in Endocrinology, Frontiers in Endocrinology, Vol 13. Retrieved from <https://www.frontiersin.org/articles/10.3389/fendo.2022.900499/full>.

- "Overview of Maternal Health Conditions and Associated Risks during Pregnancy." pub.mdpi-res.com, 21 July 2025, [https://pub.mdpi-res.com/medicina/medicina-61-01077/article\\_deploy/html/images/medicina-61-01077-g001.png?1749700192](https://pub.mdpi-res.com/medicina/medicina-61-01077/article_deploy/html/images/medicina-61-01077-g001.png?1749700192).