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Advances In Maternal–Fetal Health Research: Genetic Variants, Image Processing Biomarkers, And Their Implications For Pregnancy Outcomes And Paediatric Development

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Abstract
Maternal–fetal health research is increasingly moving toward integrated models that combine genetic, molecular, imaging, and clinical biomarkers to improve the prediction of pregnancy outcomes and pediatric development. Adverse pregnancy outcomes such as preeclampsia, fetal growth restriction, preterm birth, gestational diabetes, placental insufficiency, congenital anomalies, and neurodevelopmental vulnerability often arise from complex interactions among maternal physiology, fetal genetic contribution, placental function, environmental exposure, and healthcare context. This review examines advances in genetic variants, epigenetic regulation, image processing biomarkers, and imaging–genomics integration in maternal–fetal medicine. Genetic and molecular markers provide insight into disease susceptibility, placental programming, inflammatory regulation, metabolic dysfunction, and developmental risk, while ultrasound, Doppler imaging, placental MRI, fetal MRI, radiomics, and artificial intelligence–based image analysis offer non-invasive approaches for monitoring fetal and placental status. The review also discusses how integrated biomarker strategies may support precision maternal–fetal medicine through personalized surveillance, risk-based monitoring, biomarker-guided prevention, and improved neonatal and pediatric planning. Although these advances show strong translational potential, clinical implementation remains limited by biomarker heterogeneity, validation gaps, population diversity, ethical concerns, and the need for longitudinal mother–child outcome data. Future maternal–fetal research should prioritize multi-center, multi-modal studies that integrate genetics, imaging, environmental exposures, and pediatric follow-up to strengthen prediction, prevention, and personalized care across pregnancy and early development.

Keywords: Maternal–fetal health; Genetic variants; Image processing biomarkers; Pregnancy outcomes; Pediatric development.

1. Introduction

The study of maternal-fetal health is moving into a new era where pregnancy is viewed as a dynamic process that influences and is influenced by maternal physiology, placental function, fetal development, neonatal outcomes, and pediatric health. Although the clinical risk factors, routine biochemical screening, ultrasound surveillance, and maternal history have been used for a long time in traditional obstetric assessment, they may not adequately reflect the complexity of the molecular and developmental mechanisms that underlie adverse pregnancy outcomes. Preeclampsia, fetal growth restriction, preterm birth, gestational diabetes (GDM), chromosomal abnormalities, placental insufficiency, and impaired fetal development are frequent complications that are due to a combination of maternal biology, fetal genetic contribution, placental adaptation, environmental exposures and access to health care. Hence, there is a need for novel strategies to study the molecular biology, genetics, imaging sciences, machine learning, and precision medicine to enhance the prediction, monitoring, and intervention of pregnancy.

Early prediction of pregnancy complications is of increasing importance because many complications are slow developing, and there are no clinical signs until the events have occurred. The present method of maternal-fetal surveillance frequently identifies the risk after the placental dysfunction, fetal compromise or metabolic disturbance is already advanced. With the progress of machine learning, there are new opportunities to combine clinical, biochemical, imaging and molecular variables to better risk stratify diseases and complications of pregnancy. These methods could potentially be used to detect high-risk pregnancies at an early stage, to aid individualised monitoring and, together with clinically actionable biomakers, to inform decisions in maternal–fetal medicine (Mennickent et al., 2023).

In addition, genetic and omics-based methods have also helped to increase the understanding of the maternal–fetal interface. Pregnancy is influenced by a series of interactions between maternal genome, fetal genome, placental transcriptome, epigenome, metabolome, proteome and immune environment. These biological layers affect the implantation, vascular remodeling of the placenta, immune tolerance, nutrient transfer, fetal growth and developmental programming. Thus, omics research has emerged as a central tool in understanding the role of maternal–fetal interactions in shaping both pregnancy and developmental outcomes and has the potential to drive the developmental origins of child health and disease (Ozen et al., 2023). Additionally, maternal factors during pregnancy, such as metabolic health, obesity, glucose regulation, hypertension, inflammation, nutrition and environmental factors, further shape fetal development and can have an impact on immediate obstetric outcomes and childhood health trajectories (Muglia et al., 2022).

The placenta plays a key role in this area as it serves as a biological mediator and a predictor of fetal development. Fetal adaptation and long-term child health is affected by placental growth, vascularization, endocrine signaling, nutrient transport, immune regulation and epigenetic programming. The notion of placental programming is that the function of the placenta can influence fetal phenotype and subsequently disease susceptibility and placental biomarkers are critical to understanding associations between pregnancy conditions and paediatric development (Sferruzzi-Perri & Camm, 2016). This underlines the importance of assessing maternal, fetal and placental risk using combined molecular and imaging tools, rather than using individual clinical parameters.

Precision medicine is more and more relevant for maternal and neonatal health as it involves individual risk assessment, screening and intervention tailored to genetic, molecular, clinical and environmental data. Using precision maternal–fetal medicine can help better care by determining which patients should be monitored more closely, intervened upon sooner, or treated with special planning for the neonate. The last research on precision medicine activities in maternal and neonatal health reveals opportunities to improve genomic screening, biomarker discovery, personalized monitoring and translational research in pregnancy care (Al-Dewik et al., 2024). Concurrently, molecular detection in prenatal screening, combined with fetal evaluation and clinical interpretation, like the development of biomarkers for trisomy 18 or trisomy 21, underscores the significance of combining molecular identification with fetal characterization and clinical interpretation (Ameen & Elmetwalli, 2024).

The use of image processing biomarkers provides an additional valuable layer of information to maternal/fetal studies, as it transforms ultrasound, Doppler, placental imaging, fetal MRI data into quantitative measures of structure, growth, vascular function, and developmental risk. These biomarkers in conjunction with genetic and molecular information could be used to more effectively predict pregnancy complications and pediatric outcomes. This review thus aims at exploring recent advances in maternal–fetal health research based on genetic variants, image processing biomarkers and their association with pregnancy outcomes and pediatric development. It seeks to integrate the genetic, molecular, imaging, and precision-medicine strategies that can help to advance risk prediction, clinical translation and long-term maternal–child health.

2. Genetic Architecture of Maternal–Fetal Health

2.1 Maternal Genetic Variants and Pregnancy Risk

The maternal genetic variation is associated with pregnancy risk via metabolic, vascular, immune, inflammatory, thrombotic, and endocrine adaptations and placental interactions. These genetic factors may not be the only ones responsible and may interplay with maternal age, obesity, pre-existing disease, environmental exposure, nutrition and social determinants of health. Biological susceptibility and contextual factors affecting access to care, baseline health, stress exposure and disease risk thus affect obstetric outcomes. This integrated perspective is crucial since genetic risk can be compounded or modified by social and environmental factors, and the prediction of the health of mother and fetus is more complex than prediction based on single genes (Grobman et al., 2024).

2.2 Fetal Genetic Contributions to Developmental Outcomes

The fetal genome is directly involved in growth, organ formation, neurological development, risk of congenital anomalies and postnatal health trajectory. Additional genetic variation along neurodevelopmental pathways can impact fetal brain maturation and/or pediatric outcomes that are downstream of the fetlock, especially in the context of prenatal adversity or placental dysfunction. One of the most difficult problems in fetal-neonatal neurology is the difficulty of predicting developmental outcomes with absolute accuracy from a combination of early structural and/or molecular findings. This

uncertainty underscores the requirement for integrated diagnostic-prognostic models that take into account fetal genetics, imaging, neonatal assessment and follow-up (Scher, 2024).

2.3 Placental Genetic Regulation and Pregnancy Complications

The placenta is genetically and functionally unique as it is the product of fetal gene expression and functions in the regulation of maternal–fetal exchange. The function of genes, methylation status, vascular signals, inflammatory regulation, and endocrine activity in the placenta affects implantation, fetal growth, maintenance of pregnancy and maternal adaptation. Changes in DNA methylation are an emerging field of research in pregnancy-induced hypertension (PIH) and may play a role in the regulation of placental vascular function, endothelial response and disease progression. These data suggest a possible genetic and/or epigenetic mechanism of regulation in the placenta, which may contribute to the understanding of the difference between clinically stable and hypertensive pregnancies (Deng et al., 2024).

2.4 Gene–Environment Interactions in Maternal–Fetal Medicine

The concept of gene–environment interaction plays a key role in maternal–fetal medicine as, for example, inherited susceptibility may be influenced by obesity, nutrition, exposure to chemicals, smoking, stress, diabetes, socioeconomic factors and access to health care. One way that the environment might change the regulation of genes without changing the DNA is through epigenetic modifications. Epigenetic changes induced by obesity are of special interest given that the metabolic status of the mother has the potential to affect inflammation, insulin signaling, placental function and fetal programming. The study of obesity epigenetics is a good illustration of the general idea that metabolism and environment can modify the risk of disease by modifying DNA, modifying histones, and regulating non-coding RNAs (Wu & Yin, 2022).

2.5 Epigenetic Regulation and Developmental Programming

Epigenetic regulation offers a biological mechanism explaining the connection between exposure and the problems during pregnancy, and long-term development in children. DNA methylation, changes in chromatin accessibility and changes in the patterns of gene-expression could affect how the fetus adapts and the likelihood of developing disease later in life. Deep-learning and genomic data analytics have been more frequently used for complex developmental diseases such as neurodevelopmental diseases as they can uncover high dimensional information that is not easily captured by conventional data analysis alone (Sharma et al., 2024). In the field of maternal–fetal research, machine learning could also be used to enhance the interpretation of genetic, epigenetic, cardiovascular and physiological signals, especially in cardio-obstetrics and pregnancy physiology (Ricci et al., 2024).

2.6 Genetic Factors in Pregnancy Loss

Recurrent pregnancy loss is also a major part of the role of genetics in pregnancy, with chromosomal abnormalities, inherited variants, parental genetic contribution, immune related genes, thrombophilia related mechanisms and embryonic developmental defects all playing a role in the viability of pregnancy. It is crucial to understand these mechanisms, because it is important to know that there is not one cause of recurrent pregnancy loss, but multiple interacting biological pathways. Recent studies of genetic causes of recurrent pregnancy loss highlight the importance of better genetic screening, molecular diagnosis and tailored counseling for risk and management (Li et al., 2023).

Table 1. Key Genetic and Epigenetic Contributors to Maternal–Fetal Health

Contributor	Maternal–fetal relevance	Associated pregnancy or developmental concern	Biomarker/research implication	Sources
Maternal genetic variants	Influence vascular function, immune regulation, metabolism, inflammation, and pregnancy adaptation	Preeclampsia, gestational diabetes, recurrent pregnancy loss, fetal growth restriction	Supports individualized maternal risk assessment	Grobman et al. (2024); Li et al. (2023)
Fetal genetic variants	Affect organ formation, fetal growth, neurodevelopment, and congenital anomaly risk	Congenital anomalies, developmental delay, fetal structural abnormalities	Supports fetal genetic screening and pediatric risk prediction	Scher (2024); Sharma et al. (2024)
Placental genetic regulation	Controls trophoblast invasion, nutrient transport, endocrine signaling, and maternal–fetal exchange	Placental insufficiency, fetal growth restriction, preterm birth, stillbirth risk	Positions the placenta as a predictive biological interface	Deng et al. (2024)
DNA methylation	Regulates gene expression without altering DNA sequence	Pregnancy-induced hypertension, fetal programming, altered birth outcomes	Useful for epigenetic risk profiling	Deng et al. (2024); Wu & Yin (2022)

Gene–environment interaction	Links genetic susceptibility with obesity, nutrition, smoke exposure, pollution, stress, and healthcare access	Metabolic dysfunction, altered fetal growth, and neurodevelopmental vulnerability	Supports multi-factorial risk modeling	Grobman et al. (2024); Wu & Yin (2022)
Paternal genetic and epigenetic contribution	Influences embryo quality, sperm DNA integrity, and pregnancy viability	Recurrent pregnancy loss, early embryonic failure	Expands risk assessment beyond maternal and fetal factors	Li et al. (2023)
Multi-omics signatures	Integrate genomic, epigenomic, transcriptomic, proteomic, and metabolomic signals	Complex pregnancy complications and long-term child health outcomes	Supports precision maternal–fetal medicine	Sharma et al. (2024); Ricci et al. (2024)

3. Molecular Pathways Linking Genetic Variants to Pregnancy Outcomes

3.1 Angiogenesis and Placental Vascular Development

Genetic and molecular variation may affect pregnancy outcomes by affecting placental development, vascular remodelling, trophoblast invasion, and maternal–fetal exchange. Abnormal regulation of placental growth and vascular function may play a role in causing fetal growth restriction, hypertensive disorders, congenital abnormalities, and adverse neonatal outcomes. Circulating DNA and RNA can be used to identify noninvasive prenatal testing for fetal and placental molecular signals during pregnancy, which can be used to investigate the correlation between genomic and transcriptomic markers with placental function and fetal risk (Moufarrej et al., 2023).

3.2 Inflammation and Immune Regulation

The mechanisms of inflammation and immune regulation are major pathways involved in the maintenance of pregnancy as maternal immune tolerance must be balanced with defense against infection and tissue damage. Pregnancy loss, placental function, congenital abnormalities and developmental risk of the fetus may be related to dysregulated immune signaling. The contributions of the father to the reproductive outcome is also increasingly appreciated, including sperm DNA integrity, epigenetic state, oxidative stress and molecular factors which can influence the quality of the embryo and recurrent pregnancy loss (Kaltsas et al., 2024).

3.3 Oxidative Stress and Mitochondrial Dysfunction

Oxidative stress may connect genetic susceptibility with placental dysfunction, metabolic disturbance, and fetal injury. Excessive oxidative stress can impair cellular energy production, damage DNA, affect mitochondrial function, and disrupt fetal organ development. In pregnancies complicated by congenital cardiac conditions, maternal–fetal dynamics may involve both biological and psychological factors that affect monitoring, treatment decisions, and developmental planning. These interactions show that molecular pathways should be considered within a broader maternal–fetal context rather than as isolated mechanisms (Roy et al., 2024).

3.4 Thrombosis, Coagulation, and Endothelial Function

During pregnancy, genetic and molecular pathways involved in endothelial function, coagulation balance and vascular integrity are crucial as the maternal circulation has to adapt in order to support placental perfusion. Disruptions of these systems can lead to the increased risk of placental insufficiency, fetal compromise, and hypertensive disorders and pregnancy loss. Molecular screening has also been used to enhance prenatal risk assessment through noninvasive means, and this illustrates the ability of molecular testing to facilitate earlier detection of fetal abnormalities that could be used to change the way pregnancies are managed (Oyovwi et al., 2024).

3.5 Glucose Metabolism, Insulin Signaling, and Gestational Diabetes

Gestational diabetes mellitus is an example of ways in which pathways of maternal metabolism affect pregnancy outcomes as well as long-term maternal–child health. The risk of disease and clinical course is influenced by the interplay between genetic predisposition, insulin resistance, inflammatory changes, placental hormone activity and metabolic adaptation to postpartum. Today the view on GD is to see the ante- and post-natal period as a whole, as the metabolic state of the woman can influence fetal growth, neonatal outcome and the cardio-metabolic vulnerability later in life (Mora-Ortiz & Rivas-García, 2024).

3.6 Hormonal and Endocrine Pathways in Pregnancy Adaptation

During pregnancy, placental function, fetal growth, maternal metabolism, vascular tone and immune balance is regulated by hormonal and endocrine adaptations. Interruption of these pathways can affect the neurodevelopmental programming and the subsequent paediatric outcome. Biomarker research in autism spectrum disorder is focused on the need to identify molecular, metabolic, genetic and neurodevelopmental indicators early on in life which could help to inform the

predictions and planning of interventions in children at risk (Jensen et al., 2022). Recently, new discoveries of biomarkers for autism spectrum disorders (ASD) also bolster the importance of molecular pathways between prenatal biology, early development, and later neurobehavioral outcomes (Salloum-Asfar et al., 2023).
Figure 1 summarizes the principal molecular mechanisms linking genetic susceptibility to adverse maternal and fetal outcomes.

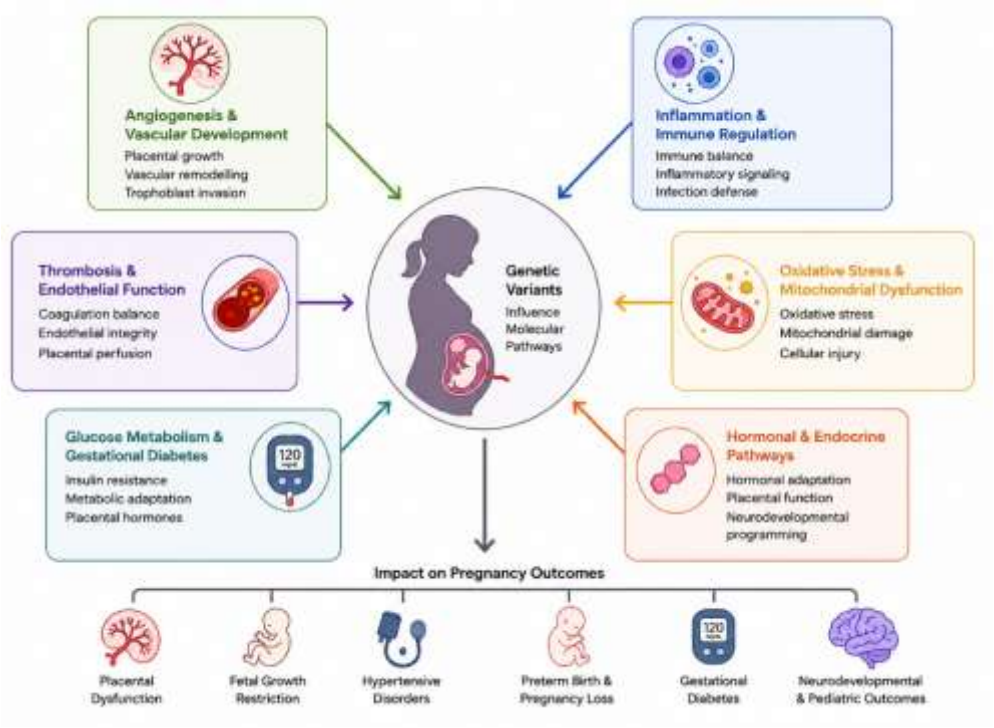

Figure 1. Molecular Pathways Linking Genetic Variants to Pregnancy Outcomes

As shown in Figure 1, alterations in vascular, inflammatory, metabolic, oxidative, endocrine, and coagulation pathways may converge to disrupt placental function and maternal–fetal homeostasis. Understanding the interaction among these mechanisms provides a biological framework for identifying predictive biomarkers and developing precision-based strategies for risk assessment, early intervention, and improved pregnancy outcomes.

4. Image Processing Biomarkers in Maternal–Fetal Assessment

4.1 Ultrasound-Based Biomarkers

Most widely used imaging modality for the maternal fetal assessment is ultrasound, which allows for real time, nondestructive, visualization of fetal anatomy, fetal growth, fetal movements, amniotic fluid volume, placenta location and fetal structural anomalies. The use of image processing has increased the utility of ultrasound for automated feature extraction, anomaly recognition, segmentation and quantitative assessment of fetal structures. Clinical engineering methods based on ultrasound imaging to recognise prenatal abnormalities are becoming more and more accepted for better consistency and early detection in diagnosis (Sriraam et al., 2024).

4.2 Doppler-Derived Vascular Indices

Doppler imaging gives functional data of uteroplacental and fetoplacental circulation, such as blood-flow resistance, vascular adaptation and fetal compromise. Doppler-derived indices may be useful in identifying abnormal placental perfusion, fetal growth restriction and hypertensive complications before clinical deterioration. Modern preeclampsia prediction strategies have been actively integrating traditional maternal risk factors, vascular markers, point-of-care screening measurements, and imaging-based markers for enhanced and early detection and management of preeclampsia (Feng & Luo, 2024). Biomarker-based and POC screening strategies could also be combined with imaging surveillance to potentially further enhance preeclampsia risk assessment (Ng et al., 2024).

4.3 Placental Imaging Biomarkers

Placental imaging biomarkers are important as the placenta is the central organ of interaction between maternal physiology and fetal development. Quantitative placental assessment can be used to provide information on placental volume,

perfusion, vascular architecture, oxygenation, texture and structural maturity of the placenta. The use of advanced magnetic resonance imaging of the human placenta has helped characterize the structure and function of the placenta, which is beyond the scope of the traditional clinical assessment, and provided insights into fetal growth restriction and congenital heart disease (Sadiku et al., 2024). In addition, the placenta is now considered a source of biomarkers for neonatal care, as its pathological, molecular and imaging traits can provide early life risk assessment (Mestan et al., 2023).

4.4 Fetal MRI and Structural Development Assessment

High resolution anatomical and functional information can be obtained by fetal MRI, complementing ultrasound findings, especially when fetal brain, thoracic, abdominal, cardiac or placental findings are uncertain. MRI-based assessment can be used to assist in the evaluation of fetal growth and organ development, placental insufficiency, and congenital abnormalities. It is particularly useful in challenging pregnancies in which ultrasound is limited due to the position of the foetus, maternal body habitus, oligohydramnios or subtle changes in foetal development. Advances in fetal and placental monitoring and the use of MRI, along with other surveillance techniques, could lead to a decrease in preventable harm by enhancing detection of fetal compromise and placental dysfunction (Ranaei-Zamani et al., 2024).

4.5 Radiomics, Texture Analysis, and Quantitative Imaging

Radiomics and texture analysis transform medical images into quantitative data that can quantify tissue heterogeneity, vascular function, structural organization and disease risk. These applications in maternal–fetal medicine include the imaging of the placenta, fetal brain evaluation, detection of fetal anomalies, and fetal growth monitoring. Quantitative imaging is especially useful as it can identify patterns that would not be noticed by traditional, visual interpretation. The current status of noninvasive prenatal screening for fetal trisomy is another example of the remarkable advancement that imaging, molecular screening, and computational interpretation can make together in order to improve clinical prenatal risk assessment (Tian et al., 2023).

4.6 Artificial Intelligence and Automated Segmentation in Obstetric Imaging

Automated segmentation and Artificial Intelligence (AI) are emerging as tools to increase the speed, reproducibility and accuracy of obstetric image interpretation. Automated tools can be used for fetal biometry, segmentation of placenta, anomaly detection, measurement of vascular structures and risk classification. These techniques can minimize observer variability and aid in the earlier diagnosis of pregnancies that would benefit from closer follow-up. But the clinical usefulness of these will require validation among populations, imaging devices, gestational ages, and clinical situations. Image processing biomarkers are therefore most valuable when they are interpretable, reproducible and coupled with genetic, molecular, and clinical markers of maternal–fetal risk.

Table 2. Image Processing Biomarkers Used in Maternal–Fetal Assessment

Imaging approach	Image processing biomarker	Maternal–fetal application	Clinical relevance	Sources
Ultrasound imaging	Automated fetal biometry, anomaly detection, structural segmentation	Assessment of fetal growth, anatomy, and prenatal anomalies	Improves early detection and reduces observer variability	Sriraam et al. (2024)
Doppler ultrasound	Uterine artery, umbilical artery, and fetal vascular indices	Evaluation of uteroplacental and fetoplacental circulation	Supports prediction of preeclampsia, fetal growth restriction, and placental insufficiency	Feng & Luo (2024); Ng et al. (2024)
Placental MRI	Placental volume, perfusion, oxygenation, vascular structure, tissue heterogeneity	Assessment of placental function and fetal growth environment	Useful in fetal growth restriction and complex placental disorders	Sadiku et al. (2024); Mestan et al. (2023)
Fetal MRI	Fetal brain volume, organ structure, and developmental morphology	Evaluation of fetal brain, cardiac, thoracic, and abdominal development	Supports prognostic assessment in congenital and developmental conditions	Sadiku et al. (2024); Ranaei-Zamani et al. (2024)
Radiomics	Texture, shape, intensity, and spatial imaging features	Quantitative assessment of fetal and placental tissue patterns	May detect subtle abnormalities not visible through routine interpretation	Tian et al. (2023); Ranaei-Zamani et al. (2024)
AI-based segmentation	Automated delineation of placenta, fetal organs, brain regions, and vascular structures	Standardized measurement and risk classification	Improves reproducibility and scalability of obstetric imaging	Sriraam et al. (2024); Ranaei-Zamani et al. (2024)

Integrated imaging biomarkers	A combination of ultrasound, Doppler, MRI, and computational features	Multi-modal assessment of pregnancy and fetal development	Supports precision monitoring and risk-based care	Ng et al. (2024); Feng & Luo (2024); Ranaei-Zamani et al. (2024)

5. Imaging–Genomics Integration in Pregnancy Risk Prediction

5.1 Concept of Imaging–Genomics in Maternal–Fetal Medicine

Imaging – genomics integration in maternal – fetal medicine is the interpretation of genetic, molecular, environment and image derived biomarkers to enhance the prediction of pregnancy risks. This is significant because adverse pregnancy outcomes are frequently due to multiple, interdependent, biological pathways and are not necessarily caused by a single abnormality. Genetics may affect placenta formation, fetal growth, vascular changes and fetal inflammatory processes, and imaging biomarkers may provide evidence of these processes during pregnancy. For Preterm birth, genetic factors, in conjunction with maternal, fetal, placental, inflammatory, and environmental factors, provide more information than single-domain predictors with integrated biomarker models (Mead et al., 2023).

5.2 Linking Genetic Variants with Imaging Phenotypes

Association of genetics and imaging phenotypes can help understand how molecular risk is manifested as fetal or placental structure. Disturbances of deep placentation have been linked to several major obstetrical syndromes, such as preeclampsia, fetal growth restriction, preterm delivery and stillbirth, which suggests that there may be a common biological basis for all these adverse outcomes (Brosens et al., 2011). Genetic or epigenetic risk markers might help to differentiate early biological risk from later clinical manifestation when used in conjunction with placental imaging features, fetal biometry, Doppler findings and indicators derived from MRI.

5.3 Multi-Modal Prediction Models for Pregnancy Complications

Pregnancy complications are frequently interpreted by taking into account a combination of maternal, molecular, fetal growth, placental and imaging markers; thus, multi-modal prediction models are increasingly relevant. A good example is preterm labor, where early recognition is hard and may require a combination of skills in cervical assessment, biochemical markers, obstetric history, inflammatory indicators as well as fetal and placental monitoring. The recent developments in early diagnosis and treatment of preterm labor indicate that an integrated approach is required to recognise preterm labour patients who might benefit from timely intervention before irreversible foetal or maternal compromise has occurred (Gondane et al., 2024).

5.4 Machine Learning Approaches for Combined Genetic and Imaging Data

Machine learning can be used for imaging–genomics integration to uncover complex patterns within high dimensional data. These models can include a genetic risk score, epigenetic imprinting, environmental factors, fetal metrics, placental imaging characteristics, and clinical parameters to calculate personalized risk estimates. But, care must be taken to validate for clinical use as prediction models could vary by population, imaging system, genetic background and health system. Additionally, prenatal environmental exposure research demonstrates that pregnancy and child-health outcomes are influenced by a variety of biopsychosocial and environmental factors, which argues for the use of models that can allow for multiple layers of data to be incorporated, not just one type of biomarker (Barrett et al., 2024).

5.5 Potential for Precision Maternal–Fetal Risk Stratification

Combining genetic and imaging biomarkers shows great promise in precision maternal–fetal risk stratification. In fetal anomaly diagnosis, the genetic result, fetal imaging, prognosis, parental counselling and ethics are all tightly interwoven, particularly if the results may impact on the outcome of the fetus or even postnatal intervention (Graf et al., 2023). Integrated assessment is also important for long-term pediatric prediction as there are efforts showing that fetal brain volume predicts neurodevelopment in CHD, indicating that fetal imaging biomarkers may provide clinically meaningful developmental information (Sadhwani et al., 2022). In addition, the link between prenatal risk, genetic diagnosis, and developmental outcome in childhood is further strengthened by genetic testing for global developmental delay in early childhood (Zhang et al., 2024). Figure 2 presents the conceptual workflow of imaging–genomics integration for pregnancy risk prediction and precision maternal–fetal care.

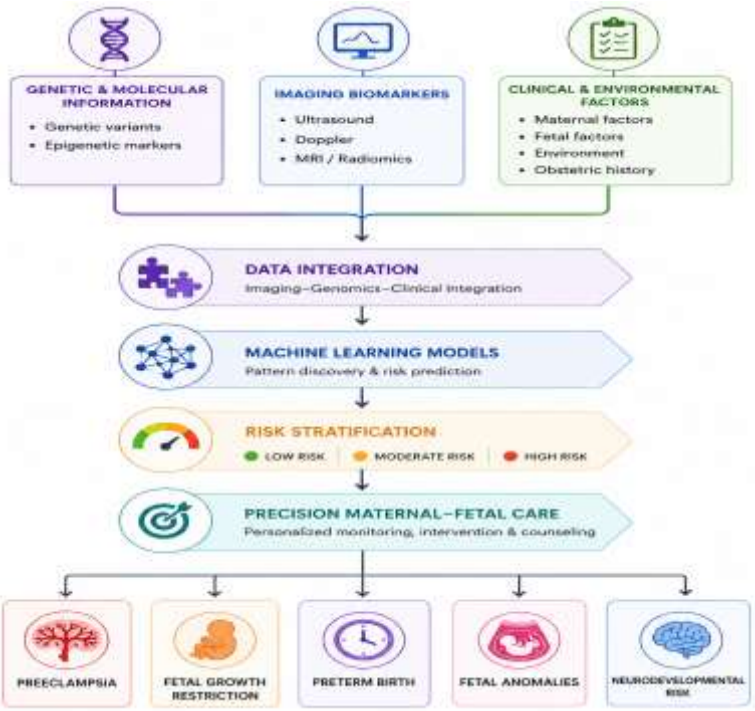

Figure 2: Integrated Imaging- Genomics Model for Pregnancy Risk Prediction

As illustrated in Figure 2, imaging–genomics integration provides a comprehensive approach for assessing maternal–fetal risk by combining information across multiple biological and clinical domains. The incorporation of machine learning techniques enables the identification of complex relationships that may not be detectable using single-marker approaches.

6. Implications for Adverse Pregnancy Outcomes

6.1 Preeclampsia

Preeclampsia is one of the most significant adverse outcomes of pregnancy due to its association with abnormalities in maternal vascular adaptations, placental dysfunction, endothelial disturbance, inflammation, and systemic organ stress. Early detection of pregnancies at risk before the onset of clinical severe disease is possible via genetic, epigenetic, inflammatory, and image-derived biomarkers. Vascular and inflammatory pathways that impact hypertensive pregnancy complications and birth outcomes may also be affected by placental methylation signatures and environmental exposures (Broseus et al., 2024).

6.2 Fetal Growth Restriction

Fetal growth restriction is tightly associated with placental insufficiency, decreased transfer of oxygen and nutrients, increased oxidative stress and fetal adaptations. Improved accuracy of diagnosis is required as late diagnosis will not allow adequate opportunities for surveillance and intervention. The findings of evidence of oxidative stress in IGR strengthen the use of molecular and placental biomarkers in understanding the neonatal complications and long-term sequelae (Nüsken et al., 2024).

6.3 Preterm Birth

Preterm birth is a multifactorial outcome, which includes genetic susceptibility, inflammation, the function of the placenta, environmental exposure, uterine activation, infection and maternal systemic condition. Biomarker-based approaches could help to improve prediction by being able to detect inflammatory or epigenetic changes prior to clinical labour. Epigenetic regulation, such as LINE-1 methylation and genes involved in pregnancy maintenance, could play a role in the molecular stability needed for a normal gestation and may help to explain mechanisms that result in early delivery and/or pregnancy disruption (Tisato et al., 2024).

6.4 Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is associated with consequences for maternal health, foetal growth, neonatal metabolic adaptation and long-term cardiometabolic risk. Genetic and inflammatory mechanisms can lead to insulin resistance, beta cell stress, placental endocrine signalling and foetal nutrient exposure. These pathways are significant as

understanding them can provide a means to reduce the risk of future metabolic vulnerability to the mother and child as well as being a complication of pregnancy (Ray et al., 2024).

6.5 Placental Insufficiency and Stillbirth Risk

Placental insufficiency is a shared pathway across several adverse outcomes, including fetal growth restriction, hypertensive disease, preterm birth, and stillbirth risk. Biomarkers that reflect placental function, fetal stress, inflammatory activation, or altered fetal adaptation may support earlier risk classification. Non-invasive clinical markers are increasingly being explored in neonatal and perinatal settings to improve diagnostic accuracy and predictive validity, showing the broader value of measurable biological signals in identifying vulnerable infants and pregnancies (Maylott et al., 2024).

6.6 Congenital Anomalies and Structural Development

Congenital anomalies and structural development changes can have long-term effects on pediatric outcomes, particularly if biological risk occurs in utero and neural vulnerability is present. Neurodevelopmental conditions like autism spectrum disorder are now thought to be caused by biological mechanisms, including a genetic susceptibility, immune regulation, metabolic signaling, and disruption in early development (Wang et al., 2023). This could also pave the way for future research on autism spectrum disorders (ASD) as a potential tool to use in larger studies on maternal-fetal research, as future biomarkers could be used to identify developmental risks earlier and create intervention plans (Mustafa, 2024).

Table 3. Biomarkers and Mechanisms Linked to Adverse Pregnancy Outcomes

Adverse outcome	Key biological mechanisms	Relevant biomarkers	Clinical implication	Sources
Preeclampsia	Abnormal placentation, endothelial dysfunction, inflammation, angiogenic imbalance, epigenetic dysregulation	Placental methylation markers, vascular indices, angiogenic biomarkers, blood pressure trends	Earlier prediction may improve surveillance and prevention of severe maternal–fetal complications	Broseus et al. (2024); Tisato et al. (2024)
Fetal growth restriction	Placental insufficiency, impaired nutrient transfer, oxidative stress, vascular dysfunction	Doppler abnormalities, placental MRI features, fetal growth parameters, oxidative stress markers	Supports closer fetal monitoring and timely delivery planning	Nüsken et al. (2024)
Preterm birth	Genetic susceptibility, inflammation, uterine activation, cervical remodeling, placental dysfunction	Genetic risk markers, inflammatory signals, cervical measures, fetal/placental monitoring	Improves early risk classification and targeted intervention	Tisato et al. (2024); Broseus et al. (2024)
Gestational diabetes mellitus	Insulin resistance, beta-cell dysfunction, placental endocrine signaling, inflammation	Glucose markers, inflammatory biomarkers, metabolic profiles, fetal growth patterns	Supports maternal metabolic monitoring and neonatal risk planning	Ray et al. (2024)
Placental insufficiency and stillbirth risk	Reduced perfusion, vascular maldevelopment, fetal hypoxia, placental aging	Doppler indices, placental imaging biomarkers, fetal movement/growth patterns, molecular placental markers	Helps identify pregnancies requiring intensified surveillance	Nüsken et al. (2024); Maylott et al. (2024)
Congenital anomalies	Genetic abnormalities, developmental disruption, structural malformation, altered fetal organogenesis	Fetal imaging findings, chromosomal screening, genetic testing, anomaly-specific markers	Supports prenatal counseling, delivery planning, and pediatric care preparation	Wang et al. (2023)
Pediatric developmental vulnerability	Fetal programming, placental dysfunction, inflammation, environmental exposure, epigenetic alteration	Neuroimaging markers, developmental biomarkers, DNA methylation signatures, early clinical indicators	Enables early developmental surveillance and intervention after high-risk pregnancy	Wang et al. (2023); Mustafa (2024); Maylott et al. (2024)

7. Implications for Pediatric Development

7.1 Fetal Programming and Long-Term Child Health

Prenatal biological factors can have a profound impact on childhood development, as fetal growth, placental development, maternal health, in-utero exposure and molecular signaling can affect long-term childhood outcomes. Fetal programming is the prenatal environment's effect on later physiological, metabolic, neurological and immune development. The placental function plays a key role in this process and is responsible for nutrient transfer, oxygen supply, endocrine signaling, immune communication and fetal adaptation. Single-cell analysis of maternal–fetal cross-talk in the human

placenta has shed new light into cellular cross-talk that occurs throughout pregnancy and has at parturition, revealing a close association between placental biology, developmental timing and fetal readiness for life after birth (Garcia-Flores et al., 2024).

7.2 Neurodevelopmental Outcomes

Maternal vascular disease, placental insufficiency, inflammation, metabolic stress, environmental exposures and fetal genetic susceptibility may influence neurodevelopmental outcome. Preeclampsia is particularly relevant, as it is associated with decreased placental perfusion, which could lead to impaired fetal oxygenation, inflammatory signals and growth restriction, all of which could impact brain development and postnatal vulnerability. The focus in recent years on predicting and managing preeclampsia has been a reminder of the potential damage to maternal and fetal health, justifying the need for earlier detection and lifelong developmental awareness following complex pregnancies (Chang et al., 2023).

7.3 Growth Trajectories and Metabolic Risk

Prenatal exposures can impact childhood growth patterns and metabolic risk through mechanisms of endocrine regulation, placental nutrient transfer, epigenetic programming, and inflammation. Adverse intrauterine conditions may lead to a higher risk for obesity, insulin resistance, cardiovascular dysfunction, or altered developmental growth patterns in children later in life. EWA studies have become important for connecting prenatal environmental exposures with long-term health outcomes as the studies can identify molecular signatures that do not occur at birth and could further elucidate developmental programming over the life course (Bakulski et al., 2023).

7.4 Cardiovascular and Endocrine Development

The cardiovascular and endocrine development can be influenced by fetal exposure to maternal hypertension, diabetes, obesity, placental insufficiency and inflammatory stress. Such prenatal influences can impact vascular structure, cardiac workload, insulin sensitivity, hypothalamic–pituitary regulation, and metabolic adaptation after birth. However, given the integration of genomic, epigenomic, transcriptomic, proteomic, metabolomic, and clinical data, there is a growing need for multi-omics and machine learning approaches to understanding female reproductive health, which can be incorporated into predictive models. These strategies can ultimately help identify pregnancies at risk of long-term cardiometabolic vulnerability in children (Kharb & Joshi, 2023).

7.5 Immune Development and Inflammatory Susceptibility

Immunity starts during fetal life and is shaped by maternal inflammatory signals, placenta expression, infection, metabolic changes, environment and genes. Altered maternal–fetal immune communication could have an impact on neonatal immune maturation and subsequent risk of inflammatory or immune-mediated diseases. Integrated biomarker research is thus of importance, as paediatric development cannot be divorced from the in-utero environment in which fetal immune, nervous, endocrine and metabolic systems are created. There is a potential for using genetic variants in combination with image processing biomarkers, to predict pediatric outcomes and identify children who need to be monitored more closely following high-risk pregnancies. Figure 3 summarizes the relationship between prenatal influences and major domains of pediatric development.

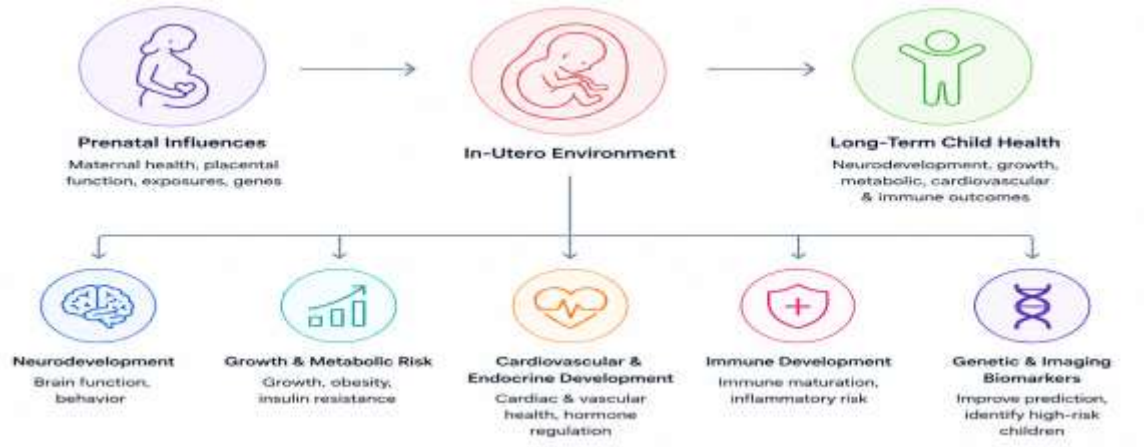

Figure 3. Prenatal Influences and Their Impact on Long-Term Pediatric Development

As illustrated in Figure 3, the intrauterine environment serves as a critical mediator between prenatal biological influences and long-term child health. Alterations in placental function, maternal physiology, immune regulation, and fetal developmental processes may have lasting consequences that extend into infancy, childhood, and later life.

8. Clinical Translation and Precision Maternal–Fetal Medicine

8.1 Personalized Surveillance and Risk-Based Monitoring

Clinical translation of genetic variants and image processing biomarkers requires a shift from uniform pregnancy monitoring toward personalized surveillance. Risk-based monitoring can help identify pregnancies requiring closer follow-up, additional imaging, molecular screening, neonatal planning, or developmental surveillance. Prenatal exposures such as maternal smoking may influence child health through DNA methylation and multi-omic changes across tissues, showing why surveillance models should account for molecular, environmental, and developmental risk together (Cosin-Tomas et al., 2022).

8.2 Biomarker-Guided Preventive Strategies

Biomarker-guided prevention may improve maternal–fetal care by identifying biological risk before clinical disease becomes advanced. Genetic, epigenetic, imaging, and environmental biomarkers can support earlier intervention for placental dysfunction, fetal growth abnormalities, neurodevelopmental risk, and metabolic vulnerability. The placental epigenome provides a molecular link between prenatal exposures and fetal health outcomes through the developmental origins of health and disease framework, making it especially relevant for preventive maternal–fetal strategies (Lapehn & Paquette, 2022).

8.3 Integration into Prenatal Screening Programs

For integrated biomarkers to become clinically useful, they must be incorporated into prenatal screening pathways in a way that is interpretable, reproducible, affordable, and ethically acceptable. Genetic testing, fetal imaging, placental assessment, and risk-prediction tools should complement rather than replace clinical judgment. Innovative in silico approaches and precision-medicine frameworks are increasingly used in personalized healthcare, supporting the development of computational tools that can assist biomarker prioritization, prediction modeling, and individualized clinical decision-making (Marques et al., 2024).

8.4 Ethical, Legal, and Equity Considerations

Precision maternal–fetal medicine raises ethical and equity concerns because genetic and imaging biomarkers can influence pregnancy counseling, risk labeling, parental decision-making, and access to specialized care. Predictive biomarkers may create anxiety if results are uncertain or poorly explained. There is also a risk that advanced genomic or imaging tools may widen health disparities if they are available only in well-resourced settings. Responsible translation requires transparent communication, culturally sensitive counseling, privacy protection, equitable access, and validation across diverse populations.

8.5 Implementation Barriers in Clinical Practice

Implementation remains challenging because integrated biomarker systems require standardized data collection, validated algorithms, trained clinicians, interoperable health records, and clear clinical action thresholds. Neuroimaging genetics demonstrates how combining imaging and genetic data can support early biomarker discovery for developmental conditions, but it also highlights the need for careful validation before clinical application (Nisar & Haris, 2023). In maternal–fetal medicine, future clinical translation will depend on whether integrated genetic and imaging biomarkers can improve outcomes beyond existing screening methods while remaining practical, explainable, and accessible. Figure 4 summarizes the potential application of integrated biomarker-based risk assessment for improving maternal, fetal, and long-term pediatric outcomes.

Figure 4: Integrated Biomarker-Based Framework for Maternal, Fetal, and Pediatric Outcome Prediction

As illustrated in Figure 4, integrated biomarker approaches have the potential to support precision maternal–fetal healthcare through individualized risk assessment and targeted intervention strategies. The incorporation of genetic, imaging, clinical, and environmental information may facilitate earlier identification of vulnerable pregnancies and improve monitoring throughout the prenatal period.

9. Challenges and Future Directions

Although there have been tremendous advances in maternal–fetal genetics, image processing biomarkers, and precision medicine, there are still a number of hurdles that prevent clinical translation. A major challenge is the absence of uniform biomarker definitions in the different studies. Different platforms, protocols, populations and analytical methods are commonly used, which may result in the generation of different genetic variants, epigenetic signatures, ultrasound parameters, Doppler indices, placental MRI features and radiomic measurements. This makes it hard to compare results from cohort to cohort, or draw models that can be applied to everyone. In Q1 maternal fetal research, it is crucial that the results are reproducible and externally validated as the performance of biomarkers could differ with various ancestries, maternal ages, comorbidities, socioeconomic status, access to healthcare, gestational ages, and imaging quality. One crucial issue is the ability to combine complex multimodal data to clinically useful tools. while genetic and imaging biomarkers might enhance risk prediction, their utility will rely on their interpretability/usefulness, cost-effectiveness, accessibility and clear clinical action pathways. Mathematically strong but clinically opaque prediction models might not be easily applicable to obstetric care. Before these tools can therefore be used to guide surveillance or intervention, explainable artificial intelligence, transparent model reporting, and prospective validation are therefore necessary. The ethical issues also persist, especially if the predictive data is concerning fetal anomalies, risk of disease development in childhood, or susceptibility to disease in the future. Families need to be counselled carefully to ensure that the biomarker-based risk estimates do not beget unnecessary anxiety or deterministic interpretations. Future studies should focus on large, diverse, multi-center longitudinal cohorts of mothers and children beginning in early pregnancy and continuing into childhood. These studies should include maternal genetic data, fetal and placental molecular markers, ultrasound, Doppler, MRI, measures of environmental exposures, and measures of pediatric developmental outcomes. This would enable researchers to identify which biomarkers are actually predictive, which are only associative, and which sets of biomarkers offer any real improvement over the standard clinical care. Future efforts should also be directed toward harmonization of imaging protocols, advancing data-sharing agreements, global validation of imaging biomarkers, and the creation of integrated, accurate, equitable, explainable, and clinically actionable risk models.

10. Conclusion

With the development of research studies on maternal–fetal health, the importance of the interaction between maternal biology, fetal genetics, placental function, molecular regulation, environment exposure and clinical context is increasingly becoming evident for shaping pregnancy outcomes and pediatric development. Genetic variants and epigenetic mechanisms give important insight into susceptibility to pregnancy complications; image processing biomarkers give non-invasive insight into quantifying fetal growth, placental structure, vascular function and developmental risk. Together, these strategies foster a more holistic perspective on pregnancy as a biological process that spans from maternal health to fetal adaptation and long-term child development. The review emphasizes that there is great potential for the use of genetic and imaging biomarkers for the better prediction of preeclampsia, fetal growth restriction, preterm birth, gestational diabetes, placental insufficiency, congenital anomalies and pediatric developmental vulnerability. They are most useful when used in conjunction in precision maternal–fetal medicine. Integrated biomarker models could potentially aid in the earlier identification of high-risk pregnancies, individualizing surveillance, directing preventive measures, and planning for neonates and children. But careful validation, standardized protocols, population diversity, ethical implementation, and clear action pathways are required for clinical translation. Future studies should focus on multi-center longitudinal studies of combining genetic, molecular, imaging, environmental, and paediatric outcome data. A clinically relevant genetic-Image integration of genetic variants and image-derived biomarkers can enhance maternal–fetal risk prediction and facilitate improved health outcomes for both mothers and children.

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