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Review Article

Biomarker-Guided Prediction of Pregnancy Viability, Current Evidence and Emerging Insights: A Narrative Review

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Abstract

Early detection of pregnancy viability is crucial for timely intervention and optimal maternal-fetal outcomes. Biomarkers represent a promising advancement for improving diagnostic accuracy and customized patient management. Four databases were searched based on MeSH keywords; extracted data were synthesized and categorized into Cytokines, adipokines, and emerging non-classical biomarkers. For each, the mechanism of action, advantages, and limitations were discussed. Cytokines were key players in immune modulation and facilitating early embryonic growth. Adipokines mirrored the maternal metabolic-inflammatory cross-talk in early pregnancy. The non-classical biomarkers offered enhanced sensitivity by capturing subtle molecular changes that surpass those observed in clinical signs. Biomarkers gave the advantage of non-invasive risk stratification and personalized monitoring; however, they are hindered by a lack of standardization and limited integration in practice. Integrated multiomic research and leveraging machine learning are recommended as future research areas to enhance diagnostic precision and clinical translation from laboratory insights into clinical practice.

Keywords: Biomarkers, Viable pregnancy, Cytokine, Adipokine, Emerging non-classical biomarkers.

التنبؤ الموجه بالمؤشرات الحيوية لصلاحية الحمل والأدلة الحالية والرؤى الناشئة: مراجعة سردية

الخلاصة

يعد الكشف المبكر عن صلاحية الحمل أمرا بالغ الأهمية للتدخل في الوقت المناسب والنتائج المثلى للأم والجنين. تمثل المؤشرات الحيوية تقدما واعدا لتحسين دقة التشخيص وتحديد العلاج المناسب. تم البحث في أربع قواعد بيانات بناء على الكلمات الرئيسية MeSH. تم تشكيل البيانات المستخرجة وتصنيفها إلى السيتوكينات والأديبوكينات والمؤشرات الحيوية غير الكلاسيكية الناشئة. وبالنسبة لكل منها، نوقشت آلية العمل والمزايا والقيود. كانت السيتوكينات لاعبا رئيسيا في تعديل المناعة وتسهيل النمو الجنيني المبكر. عكست الأديبوكينات الدور المتبادل الالتهابي الأيضي للأم في بداية الحمل. قدمت المؤشرات الحيوية غير الكلاسيكية حساسية معززة من خلال التقاط التغيرات الجزيئية الطفيفة التي تفوق تلك التي لوحظت في العلامات السريرية. أعطت المؤشرات الحيوية ميزة التقسيم الطبقي للمخاطر غير الغازية والمراقبة الشخصية. ومع ذلك، فإن الافتقار إلى التوحيد القياسي والتكامل المحدود في الممارسة العملية يعوقونها. يوصى بالبحث المتكامل متعدد الأتجاهات والاستفادة من التعلم الآلي كمجالات بحثية مستقبلية لتعزيز دقة التشخيص والترجمة السريرية من الرؤى المختبرية إلى الممارسة السريرية.

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INTRODUCTION

Accurate prediction of early pregnancy viability is critical to optimize reproductive care, guide clinical decisions, and minimize the emotional and financial burden of pregnancy loss [1]. A pregnancy is deemed viable when there is a reasonable expectation of progression toward live birth, as documented by ultrasound findings and clinical parameters in early pregnancy, based on ACOG guidelines (as outlined by the American College of Obstetricians and Gynecologists) [2,3]. A giant leap in ultrasound technology has significantly improved imaging capabilities for the early detection of viable pregnancies. Still, the combination of imaging with serial beta hCG to track early pregnancy viability often lacks sensitivity and specificity to distinguish viable vs. non-viable pregnancy, especially in the early stages of implantation [4,5]. For this, there was a need for reliable, non-invasive biomarkers that could accurately predict implantation success and healthy gestation progress.

Early embryonic development

During the first and early second trimesters of pregnancy, the early embryonic development that occurs [including implantation and placentation] has comparable inflammatory reactions with molecular and cellular features similar to those of open wounds. After the blastocyst implants itself through the uterine epithelial lining, causing a localized disruption of the lining, in the following stages of embryonic development, the trophoblast layers of the blastocyst will invade and remodel the maternal spiral arteries to replace the uterine endothelium and maternal vascular smooth muscle cells, thereby forming the best optimal fetomaternal interfaces. This process will initiate a sustained, well-controlled inflammatory response that guarantees tissue remodeling,

clearance of cellular debris, and restoration of endometrial integrity. Simultaneously, the mother's body undergoes a number of physiological changes, including the activation of immunotolerance mechanisms and hormonal modulation, as it attempts to accommodate and adapt to the growing fetus [6]. Pre-implanted embryos produce a range of cytokines, including IL-6, epidermal growth factor [EGF], and basic fibroblast growth factor, which help the embryo and mother integrate at the implantation sites. Heparin-binding EGF is thought to be secreted by the uterine epithelium and has a crucial role in blastocyst implantation and growth fromthe moment of blastocyst attachment to the uterine wall [7]. Other important cytokines that mediate the implantation process and facilitate modulation of the immune response at the feto-maternal interface include leukemia inhibitory factor [LIF]-like cytokines and elements of the IL-1 system [IL-1α, IL-1β, IL-1 receptors]. Having a successful pregnancy relies on a finely tuned balance between pro-inflammatory and anti-inflammatory signals, orchestrated by carefully regulated endocrine and immune mechanisms. Such balance ensures that the mother's immune system can tolerate the growing fetus, supporting fetal implantation, placental development, and fetal growth [8].

Biomarkers and mechanisms involved in early pregnancy

Cytokines and adipokines play a crucial role in this process and are recommended as biomarkers for predicting pregnancy viability due to their key roles in modulating immune tolerance, trophoblast invasion, endometrial receptivity, and metabolic adaptation [9,10]. Cytokines are immunological signaling peptides that orchestrate trophoblast invasion, angiogenesis, and maternal immune tolerance. The main constituents of the adaptive immune system are helper T [Th] cells, which are typically grouped according to their cytokine secretion profiles and immune system roles. An essential function of type 1 helper T cells [Th1] is intracellular protection against pathogens, while type 2 helper T cells [Th2] are in charge of both allergic reactions and parasite infection responses [11,12]. The type of cytokine that dominates will likely determine the pregnancy outcome. For example, the Th2-dominant cytokine promotes embryo implantation and supports a healthy pregnancy. In contrast, Th1-dominant cytokine is linked with implantation failure and early pregnancy loss [13]. Adipose tissue is increasingly recognized as a distinct and metabolically active organ system that has an integral role in endocrine signaling, immune modulation, and energy metabolism [14]. It is mainly composed of adipocytes, immune cells, fibroblasts, and other hormone-secreting cells that release cytokines and adipokines. The latter are a class of bioactive proteins functioning as hormones and cytokines that regulate diverse functions in the human body, including inflammation, metabolism, and reproduction, as well as early pregnancy development, where they promote placenta development and embryo-maternal communication [15-17]. There are additional subclasses of biomarkers called emerging non-classical biomarkers, such as microRNA. These are detected in maternal blood, follicular fluid, or the embryo culture period. They play an integral role in early implantation and placentation, which reflects embryonic viability. Certain types were associated with ectopic pregnancy and miscarriage. In assisted reproduction ART, they were employed in assessing oocyte and embryo quality, which underscores their role in assessing pregnancy viability [18,19]. The harmonic expression of these biomarkers mirrors the immune-metabolic environment required for healthy implantation and early embryonic development. Deviating from this fine-tuned balance increases the odds of pregnancy loss, making them promising biomarkers for predicting early pregnancy viability [20] (Figure 1).

Figure 1: The role of cytokine and adipokine in fine-tuning for early pregnancy.

A notable knowledge gap exists in the lack of an integrated, comprehensive analysis examining adipokines and cytokines in the context of early pregnancy viability [21]. Their clinical application in practice is further hampered by inconsistent validation, the absence of standardized protocols, and fragmented research design. Furthermore, a few studies correlate these biomarkers with a clearly defined pregnancy outcome, such as biochemical pregnancy, early pregnancy loss, or live birth [22]. Here, we aim to critically synthesize current evidence on the predictive value of selected cytokines and adipokines for early pregnancy viability. By exploring the underlying mechanism of action and assessing their predictive performance, we aim to translate that into clinical practice. Identifying research gaps will guide future research direction to support reproductive care strategies to mitigate the emotional and economic burden of early pregnancy loss.

METHODS

An online search was conducted via electronic repositories [PubMed, Scopus, WOS] for English-language clinical papers examining the role of cytokines and adipokines in early pregnancy viability for the last decade, till May 2025. An exclusion was made for animal studies, case reports, and letters. Boolean operators were used to combine keywords (such as "cytokines," "adipokines," "pregnancy viability," and "implantation") with corresponding MeSH terms. Titles, abstracts, and extracted data were screened, reviewed, and tabulated using a standardized template. Any extraction conflicts were settled by consensus. We used the PICO Framework that covers the following: 1) Population of interest: Women assessing early pregnancy viability, whether naturally conceived or by assisted reproduction technique; 2) Intervention: evaluation of cytokines and adipokines; 3) Comparison done: viable vs. non-viable pregnancies, we recorded study design, biomarker assays, sampling timepoints, and 4) Outcome measured: healthy pregnancy [implantation success, biochemical pregnancy, early pregnancy loss, live birth. As a result, the extracted data were sub-grouped into cytokines, adipokines, and innovative biomarkers. Figure 2 illustrates the study workflow.

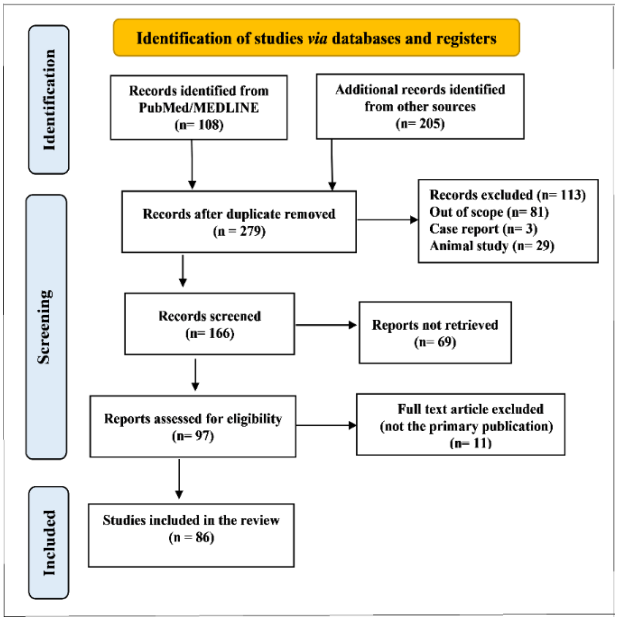

Figure 2: PRISMA flow chart of the biomarkers predict pregnancy viability.

RESULTS

Cytokine role in early pregnancy viability

Cytokines play a crucial role in immunomodulation during the early implantation stage, as reflected by their clinical use as indicators of a healthy pregnancy. Moreover, their profiles are used to stratify patients' risk for implantation failure in addition to other pregnancy complications, such as PE, PL, and GDM [23]. Incorporating patients' clinical and cytokine profiles helps identify high-risk groups, allowing for timely intervention and personalized therapeutic approaches. One of the advantages of cytokine testing is the diversity and accessibility of sample types used for analysis. Peripheral blood is most commonly used, offering a convenient, clinically familiar, and easy-to-collect method with minimally invasive procedures to assess the systemic inflammatory state [24]. Other samples, including amniotic fluid and cord blood, are employed [25]. Blood-derived cytokine panels are used to discriminate cases with immunological dysfunction manifested as early implantation failure and pregnancy loss [26]. In IVF cases, endometrial fluid and cervical-vaginal secretions are used to mirror the uterine immune environment, especially if sampling was done around the implantation window. These cytokines offer a prediction for endometrial receptivity within this time frame [27]. They have the advantage of easy sampling and a non-invasive nature, which makes it easy to integrate into fertility clinic protocols, especially for those with repeated pregnancy failures. In fetal-maternal medicine, cytokines are typically collected from blood plasma and are combined with other screening tools, such as angiogenic or placental markers. Herein, cytokine has easy accessibility, allowing risk stratification and an earlier intervention [28]. Machine learning [ML] models integrated with a cytokine profile provide personalized risk prediction with an accuracy of up to 93%. Their use is piloted in fertility centers and prenatal diagnoses to optimize decisions for complex cases [29]. We have summarized some of the cytokines that have been studied over the last decade, their biological roles, and their clinical implications, providing supporting evidence for early pregnancy loss (EPL) in Table 1.

Table 1: Biological and clinical role of cytokines in pregnancy

Cytokine	Suggested biological activity	Use in clinical practice	Reference
IL-6	Pro-inflammatory cytokine	↑ Levels were linked with EPL and implantation failure.	[30]
IL-1α	Pro-inflammatory cytokine	Embryo implantation, placenta development, and protection against infections.	[31]
IL-1β	Pro-inflammatory cytokine	Aids in trophoblast invasion and embryo implantation, but excessive expression might lead to adverse pregnancy outcomes.	[32]
IL-4	Anti-inflammatory cytokine	↑ Favor fetal survival and growth.	[33]
IL-10	Anti-inflammatory cytokine	↑ Levels were linked with implantation success and immune tolerance.	[34,35]
TNF-α	Pro-inflammatory cytokine	Disturbed levels were linked to RPL and miscarriage.	[36]
IL-17	Trigger Th1 response	↑ levels were linked to pro-inflammatory shift and seen in non-viable pregnancies.	[37]
IFN-γ	Modulate Th1 response	↑ Levels are linked to implantation failure.	[38]
IL-33	Modulate Th2 response	↓ levels are linked to miscarriage; they help implantation.	[39]
TGF-β1	Promote tissue remodeling & immune tolerance	They promote trophoblast invasion and implantation.	[40]
LIF	Pro and anti-inflammatory cytokine	Necessary for the implantation of blastocysts.	[41]
EGF	Anti-inflammatory cytokine	Implantation and embryonic development.	[26]
Irisin	Inflammatory modulator that regulates metabolism	Important in maintaining early pregnancy and was linked to successful IVF.	[42]

The adipokine role in early pregnancy

Adipokines are bioactive peptides that are primarily secreted by adipose tissue and placenta and are increasingly investigated for their role in early pregnancy implantations, pregnancy viability, and materno-fetal adaptation [43,44]. Current studies postulated that they mirror females' metabolic and inflammatory status and were linked to adverse pregnancy outcomes, especially among obese pregnancies [45,46]. The role of adipokines in reproductive medicine was examined via peripheral blood samples and follicular fluid as adjuvant biomarkers in ART. Although there were promising results, individual adipokine testing had limited predictive value in clinical practice due to inconsistent results, gestational timing, and a lack of standardization [47,48]. In feto-maternal medicine, adipokines have been found to promote placental vascularization, nutrient transport, and fetal growth patterns. Disturbances in their levels were associated with fetal growth abnormalities. It is safe to say that adipokines are yet to be integrated into clinical guidelines and are under evaluation as part of multifactorial predictive models to enhance the discrimination of high-risk pregnancies. Table 2 summarizes some adipokines and their biological activity and use in practice, along with supporting references.

Table 2: Some adipokines with their biological activity and use in clinical practice

Adipokinin	Suggested biological activity	Use in clinical practice	Reference
Leptin (pro-inflammatory cytokine)	Angiogenesis and energy metabolism.	Disturbed levels were linked to miscarriage and used to predict IVF outcome.	[49,50]
Adiponectin (anti-inflammatory cytokine)	Adiponectin suppresses pro-inflammatory cytokines, promotes M2 macrophages, protects against metabolic inflammation and insulin sensitizer.	↓ Levels were linked to early pregnancy loss and GDM.	[51,52]
Resistin (pro-inflammatory cytokine)	Immune modulator and affects IL-1β, IL-6, IL-8, IL-12 and TNF-α expression.	↑ Levels are linked to miscarriage and recurrent pregnancy loss.	[53]
Visfatin (pro-inflammatory cytokine)	An immune modulator thathas a metabolic role.	↑ Levels are linked to miscarriage and pre-eclampsia.	[54,55]
Chemerin	Metabolic regulator and promotes the secretion of pro-inflammatory cytokines such as TNF-α and IL-6, contributing to enhanced inflammation.	↑ Levels were associated with miscarriage and subfertility.	[56]
Omentin-1 (anti-inflammatory cytokine)	Anti-inflammatory, antioxidative and anti-apoptotic roles; regulates endothelial dysfunction.	↓ Levels were linked with EPL and pre-eclampsia.	[57]
Ghrelin (pro-inflammatory cytokine)	Angiogenesis and energy metabolism.	Associated with conception success; endogenous desacyl ghrelin elevates pregnancy rate and number of pups at birth.	[58,59]

Emerging non-classical biomarkers in predicting viable pregnancies

Includes multiple protein panels, microRNA metabolites, and small extracellular vesicle-derived RNA. They are gaining more recognition as early pregnancy viability detection tools [60–62]. Emerging non-classical biomarkers (ENCB) have a special advantage in practice when traditional biomarkers lack specificity or when imaging studies give ambiguous results [63]. Several studies have shown aberrant expression of microRNA in miscarriage cases (e.g., miR-323-3p, miR-517a); similarly, other proteins, such as kisspeptin, can effectively discriminate between viable and non-viable pregnancies, as well as ectopic pregnancy cases, underscoring their important role in the emergency room [64,65]. Most of the ENCBs are detected in maternal blood and can be used as an adjuvant, non-invasive tool for imaging and hormonal assessment in detecting the viability of early pregnancy. In the ART field, follicular fluid and embryo culture media, many of which were linked to oocyte quality, embryo implantation potential, and live birth prediction. What is unique about ENCB in the ART field is its predictive utility, even before the embryo is transferred, which helps guide clinicians' decisions[66]. Within feto-maternal medicine, ENCB continues to improve our understanding of placental function, immune tolerance, and vascular adaptation. Some of them were linked to PE prediction, GDM, while others were linked to FGR, which serves as a promising real-time risk stratification tool [64,67]. While emerging biomarkers offer transformative potential, their implementation in practice is hindered by limited validation, heterogeneity of sampling methods, and the population studied. With further validation, they are expected to pave the way for more precise prediction of pregnancy outcome [68]. Table 3 discusses some of the ENCB used.

DISCUSSION

Our understanding of early pregnancy viability has advanced significantly over the last decade through the study of newer biomarkers, including cytokines, adipokines, and emerging non-classical biomarkers. Research has progressively shifted from exploratory observations to mechanistically grounded investigations supported by multi-omics technology and computational modeling [81]. New biomarkers have elucidated key immune-metabolic interactions at the maternal-fetal interface, uncovering novel pathways that enable earlier, noninvasive assessment of pregnancy viability. Pro-inflammatory and anti-inflammatory immune responses interact dynamically during pregnancy, with the relative importance of each depending on the particular gestational stage. Numerous immunomodulatory cytokines are now recognized not as inflammatory mediators but as dynamic regulators of trophoblastic

invasion, implantation, and modulators of maternal immunity. A high-throughput multiplex assay enables the simultaneous assessment of cytokine panels to capture the early immunological status of pregnancy. Such an approach is of special value for cases suffering from immune dysregulation that are commonly seen in recurrent pregnancy loss and PE [82]. Adipokines are increasingly recognized for their dual action in inflammation and metabolism [83].

Table 3: Emerging non-classical biomarkers in viable pregnancy prediction (Last 10 years)

Non-classical biomarkers	Suggested biological activity	Use in clinical practice	Reference
micro RNA (**Mir-125a**)	Trophoblast invasion, immunological tolerance by modulating key genes involved in implantation.	Diagnostic biomarker, predictor of IVF setting, marker of endometrial receptivity.	[69]
micro RNA (**Mir-146a**)	Immune modulator and anti-apoptotic action.	prediction of early pregnancy failure, possible therapeutic role in recurrent pregnancy loss via its immunomodulatory role.	[70]
microRNA (**MiR-323-3p**)	Immune modulator and anti-apoptotic action.	↑ Levels were associated with miscarriage and ectopic pregnancies.	[18]
micro RNA (**MiR-517a**)	Placental development and function.	↓ Levels were associated with miscarriage and ectopic pregnancies.	[18]
α1-Antitrypsin (A1AT)	A protease inhibitor that modulates inflammation.	↓ Levels were linked to early pregnancy loss and preterm labor.	[71]
Copeptin	A stress biomarker and surrogate for vasopressin.	↑ Levels were associated with miscarriage and ectopic pregnancies.	[72]
Kisspeptin	Regulate trophoblast invasion and placental function.	↓ Levels predicted early pregnancy failure and abnormal placentation.	[65,73]
Irisin	Inflammatory modulator that regulates metabolism.	Important in maintaining early pregnancy and was linked to successful IVF.	[74]
Fibroblast Growth Factor 13 (FGF13)	Regulate cell growth, cell migration, and early embryonic development.	A marker for successful implantation and placental growth.	[75,76]
sFlt-1/PlGF Ratio	Indicator for angiogenesis imbalance.	Clinical marker for early pregnancy viability and PE.	[77]
Galectin-9	An immune checkpoint protein that promotes immune tolerance.	↓ Levels were linked to early pregnancy loss.	[78]
8-Hydroxy-2'-deoxyguanosine (8-OHdG)	A marker for oxidative stress and DNA damage.	↑ Levels were associated with miscarriage and IVF failure.	[79]
Heat Shock Protein 70 (HSP70)	Immunomodulatory and cytoprotective function.	↑ Levels were associated with early miscarriage.	[80]

Their levels not only reflect maternal energy reserve but also modulate uterine remodeling and endometrial receptivity. Impaired adipokine levels, which are often seen among obese and PCO cases, were linked to higher miscarriage odds and impaired implantation [20,55]. Understanding the significance of these chemicals may lead to more targeted interventions that enhance reproductive health and pregnancy success rates in those who are afflicted [84,85]. Research on adipokines and cytokines has evolved towards translational applications, with pilot studies now exploring their profiles in serum and uterine fluid as a novel tool for early pregnancy viability. Although these biomarkers are not yet integrated into routine practice, these studies set the groundwork for future predictive algorithms and personalized reproductive care [86]. Emerging non-classical biomarkers, such as miRNA, have emerged as key regulators in reproductive biology. Understanding the significance of these chemicals may lead to more targeted interventions that enhance reproductive health and pregnancy success rates in those who are afflicted [84]. Notably, miR-125a and miR-146a have gained recognition as critical modulators of pathways [LIFR signaling and FAS-mediated apoptosis], thus affecting embryo-endometrium cross-talk. MiRNAs hold significant promise, especially in ART settings where embryo selection is vital for improving implantation outcomes [87–90]. It is worth mentioning that integrating biomarkers into AI predictive models has produced optimistic results. A machine learning algorithm analyzing cytokine profiling can discriminate between normal and complicated pregnancies with an accuracy of 94%, thus outperforming traditional metrics by capturing nonlinear interactions and complex biochemical signatures [91,92]. This advanced approach not only enhances the accuracy of pregnancy forecasts but also paves the way for personalized reproductive medicine treatment plans. Artificial intelligence and biomarker analysis working together could transform assisted reproductive technologies, resulting in healthier pregnancies and higher success rates as research advances [93]. At the same time, the use of biomarkers in the early detection of pregnancy viability had its. As an importantant advantage, it does have some challenges that hinder the application of these biomarkers in practice, as summarized in Figure 3 and described in detail in Table 4. The inclusion of newer biomarkers, along with maternal risk factors and hormonal parameters, holds promise for refining early pregnancy risk stratification. The current expansion in ELISA kits and high-throughput multiplex assays enables a cost-effective implementation in daily practice [103]. In reproductive medicine and ART, multiplex cytokine and miRNA signatures are emerging tools that are likely to guide embryo transfer timing and tailor immunotherapy in RPL cases for more personalized therapy for subfertile couples [89]. Future studies should concentrate on multicentric longitudinal studies that encompass diverse ethnic and demographic populations to confirm their validity and predictive performance. A newer study protocol should have standardized sampling windows and assay platforms, in addition to defining interpretation thresholds to ensure reproducibility and accuracy. Simplified, rapid assay versions are needed for implementation in daily practice, especially in high-demand settings; these recommendations and more are summarized in Figure 4.

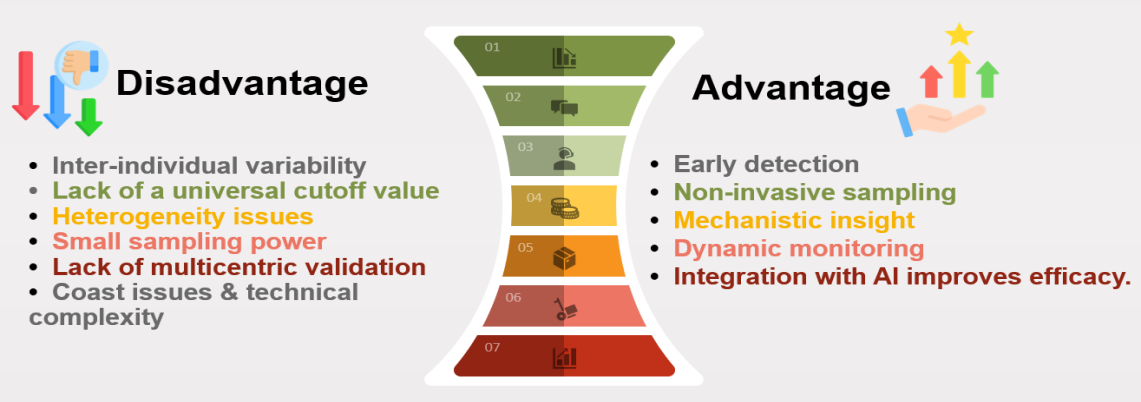

Figure 3: Advantages and disadvantages of biochemical markers.

Table 4: Advantages and limitations of biomarkers

Advantage	Description	Reference
Early detection	They are detectable before clinical symptoms manifest, as evidenced by shifts in cytokines during the first trimester.	[94]
Non-invasive sampling	They can be easily measured in peripheral blood or endometrial secretion.	[95]
Mechanistic insight	They mirror the patient's pathophysiological states: immune dysregulation, oxidative stress, and inflammation.	[96,97]
Dynamic monitoring	Their levels enable longitudinal assessment for pregnancy progression.	[98]
Integration with AI improves efficacy.	By incorporating it into machine learning models, predictions are enhanced, and accuracy is improved.	[29]
Limitation	**Description**	**Reference**
Inter-individual variability	Several patient factors, including BMI, ethnicity, and gestational age, can influence biomarker levels.	[99]
Lack of a universal cutoff value	Most of these biomarkers lack a standardized threshold for interpretation.	[100]
heterogeneity issues	Differences in lab methods used hinder reproducibility.	[101]
Small sampling power	Most studies lack diversity in the population included and have a limited scale.	[102]
heterogeneity issues	Differences in lab methods used hinder reproducibility.	[103]

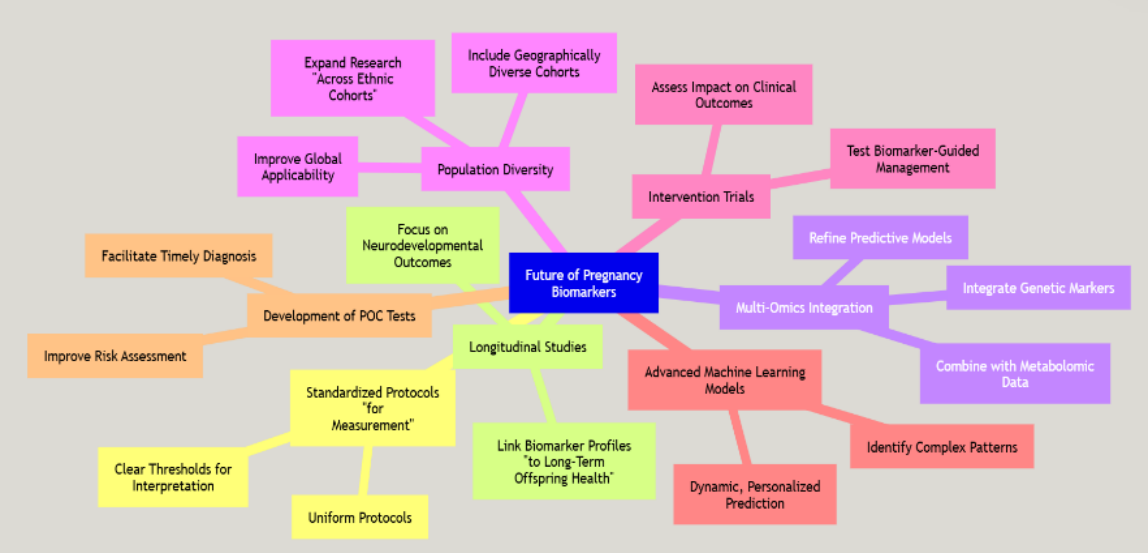

Figure 4: Summary of future research directions in pregnancy biomarkers.

Study limitations

This was a narrative review with qualitative data, lacking quantitative data, as seen in meta-analysis, for biomarker performance. The subject of population variability and resource disparity was not addressed, which may underrepresent the review's general applicability. Finally, given the fast pace of biomarkers and AI research, some of the cited findings may become outdated, which underscores the need for continuous updates.

Study strengths

The review addressed a diverse class of biomarkers, which provides a multidimensional view of early pregnancy viability. It highlights the clinical potential of emerging biomarkers in a real-world context, adding translational relevance. Early prenatal screening using cytokine/adipokine panels may be beneficial, particularly for women with recurrent miscarriages in the past, immune or metabolic disorders, IVF, or assisted conception. We have included up-to-date progress in the

integration of machine learning and AI models that combine these markers with clinical parameters [age, BMI, hormone levels]. The review bridges basic science with future clinical application pathways.

Conclusion

Cytokines, adipokines, and emerging biomarkers represent a new frontier in early pregnancy assessment, moving beyond associative findings to actionable clinical tools for risk stratification, prediction, and promising therapeutic interventions in clinical practice. Although the current use remains investigational to date, the synergy between system biology, high-dimensional biomarker profiling, and AI is a driving paradigm shift towards optimized obstetrical care. The continuous advancement in translational research and infrastructure will redefine how pregnancy viability is predicted, monitored, and managed. Striving to reduce fetomaternal morbidity and advancing reproductive care.

Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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