

Clinical algorithms in high-risk pregnancy: Evidence-based and regional perspectives

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Summary

Objective: To summarize contemporary clinical algorithms for the management of high-risk pregnancy and to integrate international recommendations with regional clinical experience.

Methods: Narrative review of international guidelines (ACOG, FIGO, NICE, WHO) and peer-reviewed literature, including data from Bulgarian obstetric practice.

Results: Algorithm-based management improves early risk stratification, standardizes care, and supports individualized decision-making in hypertensive disorders, gestational diabetes, fetal growth abnormalities, and combined maternal–fetal risk.

Conclusion: Clinical algorithms represent a cornerstone of modern high-risk pregnancy management. Integration of regional data enhances applicability without compromising international relevance.

Key words: Clinical algorithms, fetal growth restriction, gestational diabetes, high-risk pregnancy, preeclampsia, risk stratification



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Introduction

High-risk pregnancy remains one of the most complex and resource-intensive areas of modern obstetric care. Despite substantial advances in prenatal screening, fetal surveillance, and perinatal medicine, high-risk pregnancies continue to account for a disproportionate share of maternal and perinatal morbidity and mortality worldwide. Global epidemiological data indicate that hypertensive disorders of pregnancy, gestational diabetes mellitus, and placental dysfunction remain among the leading contributors to maternal mortality, stillbirth, and long-term offspring morbidity (Say et al. 2014; Huang et al. 2025). Demographic and epidemiological trends, including delayed childbearing, increasing prevalence of obesity, metabolic syndrome, chronic hypertension, diabetes mellitus, autoimmune disease, and the widespread use of assisted reproductive technologies, have contributed to a steady rise in the proportion

of pregnancies classified as high risk (American College of Obstetricians and Gynecologist 2020; Vogel et al. 2015; Cunningham et al. 2022).

Hypertensive disorders of pregnancy, gestational diabetes mellitus, and disorders of fetal growth remain the leading contributors to adverse pregnancy outcomes, including preterm birth, stillbirth, and long-term maternal and offspring morbidity. These conditions frequently coexist, share overlapping pathophysiological mechanisms such as endothelial dysfunction and placental maladaptation, and evolve dynamically throughout gestation, further complicating clinical decision-making (Gordijn et al. 2016; Rana et al. 2019). Consequently, obstetric care for high-risk pregnancy requires both early identification of risk and continuous reassessment, and timely coordinated intervention.

Clinical algorithms have emerged as a cornerstone of contemporary obstetric practice, offering structured, stepwise approaches to diagnosis, surveillance, and management. By integrating clinical data, laboratory parameters, imaging findings, and gestational age-specific thresholds, algorithms aim to standardize care, reduce inter-clinician variability, and improve adherence to evidence-based recommendations (Grant and Booth 2009). Algorithm-based care has been associated with improved maternal and perinatal outcomes in high-risk pregnancies, where delays in diagnosis or inconsistencies in management may have serious consequences.

International professional organizations, including ACOG, FIGO, NICE, ISUOG, and the WHO, have increasingly incorporated algorithmic frameworks into their guidelines for the management of hypertensive disorders, gestational diabetes, and fetal growth restriction (World Health Organization 2013; NICE 2019; American College of Obstetricians and Gynecologists 2020; ISUOG 2020). However, implementation of these algorithms in real-world clinical settings varies widely, influenced by local resources, healthcare organizations, and population-specific risk profiles. Regional and national experience plays a critical role in bridging the gap between global recommendations and everyday clinical practice. Data from Bulgarian obstetric centers indicate that international screening and management algorithms can be successfully adapted to regional settings, maintaining diagnostic accuracy and clinical effectiveness (Kirovakov and Gyokova 2025). Furthermore, regional research has contributed valuable insights into modifying factors such as inherited thrombophilia and oxidative stress, which may influence early screening parameters and disease progression in high-risk pregnancies (Kirovakov 2025; Kirovakov et al. 2025).

Unlike existing guideline summaries, this review integrates structured clinical algorithms with region-specific evidence from Bulgarian obstetric practice, highlighting practical adaptations, feasibility, and risk modifiers relevant to Eastern European populations.

Methodology

This review was conducted using a structured narrative approach, integrating international guidelines, peer-reviewed literature, and regional clinical experience (Ferrari 2015). Narrative reviews are particularly suited to complex clinical topics where synthesis of heterogeneous evidence, guideline recommendations,

and real-world practice is required (Grant and Booth 2009). The methodology was designed to provide a comprehensive synthesis of evidence-based clinical algorithms for high-risk pregnancy and highlight their applicability in routine obstetric care.

Literature search and selection

A systematic search was performed across multiple electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, covering the period from January 2000 to December 2025. Search terms included combinations of: “high-risk pregnancy”, “clinical algorithms”, “hypertensive disorders of pregnancy”, “gestational diabetes mellitus”, “fetal growth restriction”, “risk stratification”, and “thrombophilia”. Additional searches targeted national and regional publications to capture data from Bulgarian clinical practice.

Inclusion criteria were:

1. Original research, systematic reviews, or meta-analyses focused on the clinical management of high-risk pregnancy.
2. Publications presenting structured clinical algorithms or decision-support models.
3. Guidelines and consensus statements from recognized international organizations (ACOG, FIGO, NICE, WHO).
4. Regional studies providing evidence on implementation, feasibility, or outcomes in Bulgarian or Eastern European populations.

Exclusion criteria included:

- Case reports or small case series (<10 subjects) unless highly relevant to rare conditions.
- Articles not published in English or Bulgarian.
- Non-clinical basic science studies without translational relevance.

Data extraction and synthesis

Data were extracted independently by two reviewers and included: study design, population characteristics, algorithm components, outcomes, and evidence of feasibility in regional practice. A narrative synthesis was conducted, focusing on:

- screening strategies;
- surveillance protocols;
- intervention thresholds;
- integration of maternal and fetal risks.

Flowcharts were developed to represent algorithm pathways for hypertensive disorders, gestational diabetes mellitus, fetal growth restriction, and combined maternal-fetal risk.

Regional evidence integration

Bulgarian clinical experience was incorporated through published studies, institutional protocols, and registry data, providing practical insights into the feasibility, effectiveness, and adaptability of the algorithm (Table 1).

Definition and risk stratification

High-risk pregnancy is defined as a pregnancy in which maternal, fetal, or placental factors significantly increase the likelihood of adverse outcomes compared with the general obstetric population (Cunningham et al. 2022). Early identification of risk allows for preventive strategies, intensified surveillance, and timely intervention.

First-trimester combined screening models incorporating maternal history, biochemical markers, and uterine artery Doppler assessment have demonstrated improved predictive accuracy for preeclampsia and fetal growth restriction (Rolnik et al. 2017). In Bulgarian clinical practice, similar models have been successfully implemented, showing good concordance with international screening strategies and feasibility in routine care (Kirovakov and Gyokova 2025).

Inherited thrombophilia represents an additional modifier of obstetric risk. Alterations in first-trimester biochemical screening parameters associated with thrombophilia highlight the need for individualized early risk assessment (Kirovakov et al. 2024).

Algorithm for hypertensive disorders of pregnancy

Hypertensive disorders of pregnancy remain among the leading causes of maternal and perinatal mortality globally (Say et al. 2014). Algorithm-based management enables early diagnosis, standardized monitoring, and appropriate timing of delivery (Fig. 1).

Table 1. Overview of high-risk pregnancy clinical algorithms.

Algorithm	Key components	Evidence source	Regional / Bulgarian contribution	Level of evidence
Hypertensive disorders of pregnancy	- First-trimester risk assessment (maternal history, MAP, uterine artery Doppler, PAPP-A/hCG) - Preventive low-dose aspirin - Blood pressure monitoring - Angiogenic biomarkers (sFlt-1/PIGF) for disease progression	Rolnik et al. 2017; Zeisler et al. 2016	Implementation of first-trimester screening protocols in Bulgarian tertiary centers; integration of oxidative stress markers in risk assessment	I - II (Randomized trials, guidelines)
Gestational diabetes mellitus (GDM)	- Screening at 24–28 weeks (OGTT) - Lifestyle modification (diet, exercise) - Pharmacological therapy (insulin, oral agents) - Fetal growth surveillance (ultrasound)	ADA 2023; Landon et al. 2009; Ali 2025	Standardized treatment protocols in Bulgarian centers demonstrating reduced neonatal complications	I - II (Guidelines, RCTs)
Fetal growth restriction (FGR)	- Diagnosis via ultrasound biometric parameters - Doppler assessment (umbilical artery, MCA, ductus venosus) - Surveillance scheduling- Timing of delivery based on severity	Lees et al. 2015; Papastefanou et al. 2023	Regional data confirming Doppler-based surveillance efficacy; first-trimester predictors influenced by maternal thrombophilia	II - III (Prospective cohort, RCTs, guidelines)
Combined maternal-fetal risk	- Integrated assessment of overlapping conditions (e.g., preeclampsia + FGR, thrombophilia + recurrent pregnancy loss) - Multidisciplinary care- Individualized monitoring and intervention	Cunningham et al. 2022	Structured algorithms for inherited thrombophilia and adverse pregnancy outcomes; adaptation for local healthcare resources	II - III (Guidelines, cohort studies, expert consensus)

Table notes: MAP: Mean Arterial Pressure; PAPP-A: Pregnancy-associated plasma protein A; hCG: Human chorionic gonadotropin, sFlt-1/PIGF: Soluble fms-like tyrosine kinase-1 / Placental growth factor ratio; MCA: Middle cerebral artery.

Contemporary algorithms emphasize first-trimester screening using maternal characteristics, mean arterial pressure, uterine artery Doppler, and biochemical markers. Preventive administration of low-dose aspirin in high-risk women has been shown to significantly reduce the incidence of preterm preeclampsia (Rolnik et al. 2017). These findings underpin current international recommendations from FIGO, NICE, and ACOG. The Bulgarian Society of Obstetrics and Gynecology supports the clinical utility of first-trimester screening algorithms for both preeclampsia and fetal growth restriction, reinforcing their applicability in regional healthcare settings (Gyokova et al. 2024).

In cases of suspected disease progression, angiogenic biomarkers such as the sFlt-1/PIGF ratio further improve diagnostic accuracy and guide clinical decision-making, particularly in differentiating placental disease from other hypertensive conditions (Zeisler et al. 2016). Oxidative stress has been increasingly recognized as a contributing mechanism in hypertensive disorders of pregnancy, with potential implications for adjunctive preventive strategies incorporated into comprehensive clinical algorithms (Kirovakov 2025).

Algorithm for gestational diabetes mellitus

Gestational diabetes mellitus (GDM) affects up to 14% of pregnancies worldwide and is associated with adverse maternal and neonatal outcomes, including macrosomia, shoulder dystocia, and long-term metabolic disease (Metzger et al. 2008; Hod et al. 2025; ADA 2023; Erkul and Erbaş 2024).

Algorithm-based management includes universal screening at 24-28 weeks of gestation, typically using an oral glucose tolerance test, followed by structured lifestyle modification, pharmacological therapy when glycemic targets are not achieved, and ultrasound surveillance of fetal growth (Hillier et al. 2021). International recommendations from the ADA, WHO, and FIGO support these approaches (Fig. 1). Randomized trials have demonstrated that structured treatment protocols reduce neonatal complications and cesarean delivery rates (Landon et al. 2009). Regional experience confirms the importance of standardized algorithms in optimizing perinatal outcomes in pregnancies complicated by GDM (Boyadzhieva et al. 2012; Koleva et al. 2021)

The Bulgarian Society of Obstetrics and Gynecology gives the following recommendations regarding nutrition, nutritional supplements, and body weight in women with diabetes:

- Overweight women (BMI > 27 kg/m²) should be advised to normalize their BMI before pregnancy through diet, physical activity, and individualized measures.
- Taking 5 mg/day of folic acid is advised, starting several months before pregnancy and continuing until 12 weeks of age, in order to minimize the risks of neural tube defects (NTD). The recommended dose is higher than that for the general population because in patients with pre-pregnancy diabetes, the incidence of fetal NTD is 0.19% compared to 0.07% for the population without diabetes.
- Before pregnancy, HbA1c levels are monitored monthly.
- If necessary, therapy is intensified in order to optimize glycemic control.
- Before pregnancy, the goal is to maintain fasting blood sugar levels between 5 and 7 mmol/l and HbA1c below 6.5%.

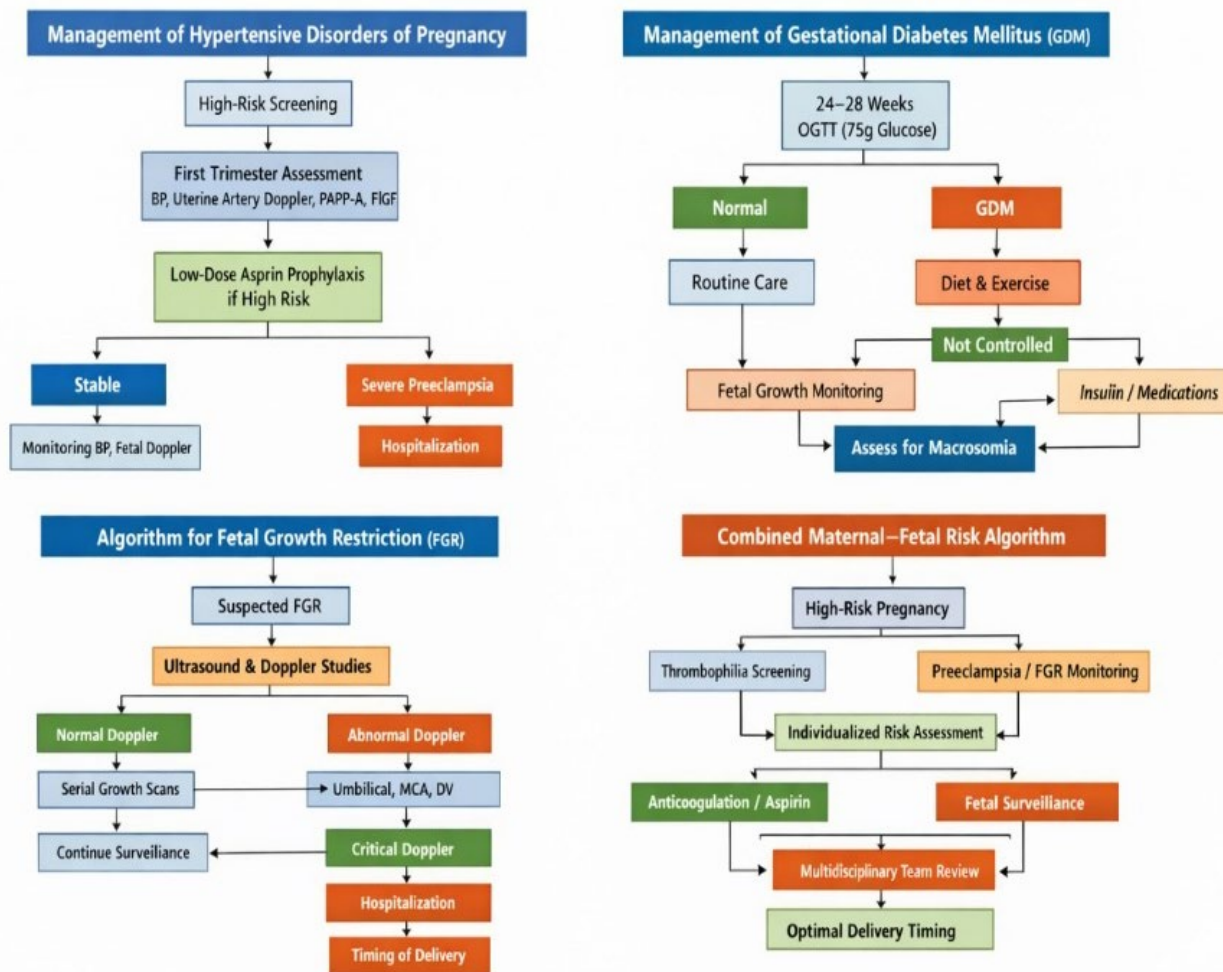


Figure 1. Algorithm-based management of hypertensive disorders and gestational diabetes mellitus.

In pregnant women with gestational diabetes mellitus and fasting blood sugar below 5.3 mmol/l, treatment with diet and a change in exercise regimen is initiated. If blood sugar normalization (fasting and postprandial) is not achieved within 1-2 weeks, insulin treatment is recommended (if insulin is refused, metformin is acceptable).

Algorithm for fetal growth abnormalities

Fetal growth restriction (FGR) is associated with increased risks of stillbirth, neonatal morbidity, and long-term cardiovascular disease. Evidence-based algorithms emphasize accurate diagnosis, Doppler-based surveillance, and individualized timing of delivery (Lees et al. 2015). Doppler ultrasound assessment of the umbilical artery, middle cerebral artery, and ductus venosus plays a central role in monitoring placental insufficiency and guiding delivery decisions, as reflected in ISUOG practice guidelines (ISUOG 2020).

National experience confirms the clinical value of Doppler-based surveillance in pregnancies complicated by fetal growth abnormalities (Yordanova-Ignatova et al. 2024). Emerging evidence suggests that first-trimester predictors, including biochemical markers influenced by inherited thrombophilia, may enhance early identification of pregnancies at risk for FGR (Kirovakov et al. 2025).

Combined maternal-fetal risk algorithms

Many high-risk pregnancies involve overlapping maternal and fetal conditions, such as preeclampsia combined with fetal growth restriction or thrombophilia associated with recurrent pregnancy loss and placental dysfunction. Integrated algorithms are particularly valuable in these complex scenarios, where single-condition guidelines may be insufficient or conflicting (NICE 2019; Cunningham et al. 2022; Papastefanou et al. 2023).

A structured algorithm for the prevention of adverse pregnancy outcomes in women with inherited thrombophilia has been proposed, emphasizing early diagnosis, targeted surveillance, and individualized intervention (Kirovakov et al. 2024). This approach aligns with international guidance from RCOG and the American College of Chest Physicians, which emphasizes risk-based thromboprophylaxis and individualized management in pregnancy (RCOG 2015; Bates et al. 2018).

Role of clinical algorithms in modern obstetrics

Clinical algorithms reduce inter-clinician variability, improve adherence to evidence-based guidelines, and enhance maternal and perinatal safety. Experience from Bulgarian tertiary centers demonstrates that algorithm-based management is feasible, clinically effective, and adaptable to local healthcare systems (Koleva et al. 2021; Kirovakov et al. 2024; Yordanova-Ignatova et al. 2024). Furthermore, standardized algorithms provide a foundation for future integration of digital decision-support tools and artificial intelligence in obstetric care.

Discussion

This review highlights the central role of clinical algorithms in the contemporary management of high-risk pregnancy, emphasizing their value in structuring care, improving early risk identification, and supporting timely clinical decision-making. As the prevalence and complexity of high-risk pregnancies continue to increase, the need for standardized yet adaptable management frameworks has become increasingly apparent. One of the key strengths of algorithm-based care is its ability to integrate multiple dimensions of risk, including maternal characteristics, biochemical markers, imaging findings, and gestation-specific thresholds. In conditions such as hypertensive disorders of pregnancy and fetal growth restriction, where disease progression may be rapid and unpredictable, structured algorithms facilitate earlier diagnosis and more consistent surveillance, which are critical for optimizing maternal and perinatal outcomes (Lees et al. 2015; Zeisler et al. 2016). The incorporation of first-trimester screening models into clinical algorithms represents a major advance in the management of high-risk pregnancies. Evidence supporting early risk stratification for preeclampsia and fetal growth restriction has led to effective preventive strategies, including low-dose aspirin prophylaxis and individualized monitoring schedules. Importantly, regional data from Bulgarian obstetric practice demonstrate that such screening algorithms can be successfully implemented outside highly specialized research settings, achieving outcomes comparable to those reported in international studies (Koleva et al. 2021), thus underscoring the generalizability of algorithm-based approaches when adapted to local healthcare systems. Another important aspect addressed in this review

is the management of overlapping maternal and fetal conditions. High-risk pregnancies frequently involve combinations of disorders, such as preeclampsia with fetal growth restriction or gestational diabetes mellitus with macrosomia. In these complex scenarios, single-condition guidelines may be insufficient or even conflicting. Integrated clinical algorithms allow prioritization of competing risks and support multidisciplinary decision-making, aligning maternal and fetal indications for intervention. Recent regional work proposing structured algorithms for inherited thrombophilia and adverse pregnancy outcomes further illustrates the potential of personalized, algorithm-guided care (Kirovakov et al. 2024).

The pathophysiological mechanisms underlying high-risk pregnancy also warrant consideration in algorithm development. Emerging evidence regarding the role of oxidative stress, endothelial dysfunction, and placental maladaptation suggests that future algorithms may benefit from incorporating mechanistic biomarkers and adjunctive preventive strategies (Kirovakov 2025). While such approaches require further validation, they represent a promising direction for enhancing the precision of obstetric care. Despite their advantages, clinical algorithms have inherent limitations. Strict adherence without consideration of individual patient context may lead to overmedicalization or delayed recognition of atypical presentations.

Additionally, variability in resource availability, particularly in low- and middle-income settings, may limit the feasibility of certain algorithm components, such as advanced biomarker testing. Therefore, algorithms should be viewed as decision-support tools that would complement, rather than replace, clinical expertise. The integration of digital health technologies and artificial intelligence represents an important future direction for algorithm-based obstetric care. Digital decision-support systems have the potential to automate risk stratification, improve adherence to guidelines, and facilitate real-time clinical decision-making. However, successful implementation will depend on robust validation, clinician engagement, and careful consideration of ethical and data governance issues.

Clinical algorithms constitute a fundamental component of modern high-risk pregnancy management. When grounded in international evidence and informed by regional clinical experience, such algorithms can enhance the consistency of care, support individualized decision-making, and improve maternal and perinatal outcomes. Ongoing refinement, validation, and contextual adaptation of these algorithms will be essential to meet the evolving challenges of contemporary obstetric practice.

On the other hand, despite their advantages, clinical algorithms have inherent limitations. As this review is based on a narrative synthesis, it may be subject to selection bias, and a heterogeneity in regional data limits direct quantitative comparison across studies. In addition, variability in healthcare resources may limit the feasibility of certain algorithm components, such as advanced biomarker testing, especially in tertiary centers outside the hospital. Nevertheless, narrative integration allows contextual interpretation of algorithm applicability in real-world practice and supports individualized clinical decision-making.

Conclusion

Clinical algorithms represent a cornerstone of contemporary high-risk pregnancy management. When aligned with international guidelines and

adapted to regional practice, they improve maternal and perinatal outcomes while supporting individualized clinical decision-making. Integration of regional evidence, including Bulgarian clinical experience, strengthens the applicability and relevance of algorithm-based obstetric care.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Use of AI

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Author contributions

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Data availability

All of the data that support the findings of this study are available in the main text or Supplementary Information.

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