Review Article

Management of Glaucoma During Pregnancy and Lactation: A Comprehensive Review

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Glaucoma in women of reproductive age is uncommon but poses significant therapeutic challenges when encountered during pregnancy and lactation. Physiological hormonal changes during pregnancy often lead to a reduction in intraocular pressure (IOP); however, disease progression may still occur, particularly in patients with pre-existing or secondary glaucomas. Treatment decisions must balance maternal visual preservation against potential fetal and neonatal risks. This review summarizes current evidence on epidemiology, physiological changes affecting IOP, and trimester-specific medical, laser, and surgical management strategies for glaucoma during pregnancy and the postpartum period.

Access this article online

Website: www.cijmr.com

DOI: 10.58999/cijmr.v5i03.434

Keywords: Glaucoma, Pregnancy, Lactation, Intraocular pressure, Antiglaucoma drugs

Introduction

Glaucoma is a chronic, progressive optic neuropathy classically associated with advancing age. It is relatively rare in women of childbearing age; however, trends toward delayed pregnancies and increasing prevalence of early-onset ocular disease have resulted in a growing number of pregnant patients requiring glaucoma management. Many such women have pre-existing glaucoma originating from childhood, including congenital glaucoma, anterior segment dysgenesis, or secondary glaucomas related to uveitis or systemic diseases such as diabetes mellitus.

Management during pregnancy is challenging due to limited clinical data, ethical considerations, and concerns regarding teratogenicity and neonatal safety of antiglaucoma medications.

Drug safety in this review is discussed according to the FDA Pregnancy and Lactation Labeling Rule (PLLR), which replaced the former pregnancy letter-category system with narrative risk summaries to facilitate individualized clinical decision-making.

Epidemiology

Data regarding the prevalence of glaucoma in women younger than 40 years are limited. A population-based Japanese study reported the prevalence of open-angle glaucoma as 0.48, 0.42, and 0.73% in women aged 15 to 24, 25 to 34, and 35 to 44 years, respectively. A German study documented a prevalence of 0.16% in individuals aged 18 to 40 years, with nearly half of affected patients being female.

A questionnaire-based survey conducted in the United Kingdom revealed that only 26% of ophthalmologists had prior experience managing glaucoma in pregnant women, while 31% expressed uncertainty regarding optimal treatment strategies. These findings highlight the lack of standardized clinical guidelines and the need for increased awareness.

Effect of Pregnancy on Intraocular Pressure

Pregnancy is generally associated with a gradual reduction in IOP, estimated to be up to 10% by the third trimester. This decrease is multifactorial and mediated by hormonal and biomechanical changes.

Hormonal Influences

Progesterone exhibits anti-glucocorticoid activity, thereby reducing the ocular hypertensive effects of endogenous corticosteroids. Estrogen enhances the production of nitric oxide, prostacyclins, endothelin-1, and eicosanoids,

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Submitted: 15/05/2026 Revision: 25/06/2026
Accepted: 05/08/2026 Published: 25/09/2026

How to cite this article: Bansod S. Management of Glaucoma During Pregnancy and Lactation: A Comprehensive Review. Central India Journal of Medical Research. 2026; 5(3):138-141.

leading to vasodilation, decreased arterial pressure, and reduced aqueous humor production. Additionally, β-hCG and relaxin reduce peripheral vascular resistance and increase aqueous outflow, contributing to lower intraocular pressure during pregnancy.

Structural Changes

Pregnancy is associated with reduced corneoscleral rigidity and increased elasticity of Schlemm's canal and the trabecular meshwork. These structural adaptations enhance aqueous outflow facility while reducing aqueous humor production, contributing to the physiological reduction in intraocular pressure observed during pregnancy. Despite these changes, some patients may experience stable or even elevated IOP, necessitating treatment.

Management Strategies

Management must be individualized and trimester-specific, with emphasis on the lowest effective dose and minimizing systemic absorption through punctal occlusion.

Medical Management

First Trimester

The first trimester carries the highest risk of teratogenesis because organogenesis occurs during this period. Consequently, initiation of medical therapy should be individualized, balancing the need to preserve maternal vision against potential fetal risks while minimizing systemic drug exposure. Brimonidine may be considered when pharmacological treatment is necessary, as available human data have not demonstrated a consistent increase in congenital malformations; however, evidence remains limited, and its use should be guided by an individualized maternal–fetal risk-benefit assessment. Because brimonidine crosses the placenta and has been associated with neonatal central nervous system depression and apnea following exposure near delivery, clinicians should anticipate the need to transition to an alternative agent and discontinue brimonidine before the late third trimester if continued intraocular pressure control is required. Topical beta-blockers may be considered when clinically indicated. Although prostaglandin analogues have theoretical uterotonic effects, available clinical evidence has not demonstrated a consistent increase in adverse pregnancy outcomes with ophthalmic use during early-to-mid pregnancy. Nevertheless, they should generally be reserved for situations in which the anticipated maternal benefit outweighs the potential fetal risk and used with greater caution during late pregnancy because of the theoretical risk of stimulating uterine contractions. Topical carbonic anhydrase inhibitors and pilocarpine should likewise be reserved for selected cases in which the anticipated maternal benefit outweighs the potential fetal risk. Although isolated reports have linked systemic carbonic anhydrase inhibitors with fetal malformations, large cohort studies have not demonstrated a statistically significant increase in congenital anomalies.

Second Trimester

Following completion of organogenesis, the risk of major congenital malformations decreases. Treatment should continue to be individualized based on disease severity and maternal–fetal risk-benefit assessment. Medications initiated during the first trimester, including brimonidine when clinically indicated, may be continued; however, clinicians should plan for transition to an alternative agent before the late third trimester because of the risk of neonatal central nervous system depression and apnea associated with exposure near delivery.

Third Trimester

During the third trimester, certain medications should be discontinued before delivery because of potential neonatal adverse effects. Brimonidine has been associated with central nervous system depression and apnea in newborns. Beta-blockers may cause neonatal bradycardia and hypotension, while carbonic anhydrase inhibitors can potentially lead to electrolyte disturbances. Pilocarpine has also been linked to rare cases of neonatal hyperthermia and seizures.

Postpartum Period and Lactation

The excretion of antiglaucoma medications into breast milk must be considered during lactation. Brimonidine should generally be avoided during lactation because of the potential risk of neonatal central nervous system depression. Pilocarpine should also be avoided because of limited safety data. Beta-blockers may be used cautiously, particularly when infants do not have underlying cardiopulmonary disease, although monitoring is advisable. Prostaglandin analogues and systemic carbonic anhydrase inhibitors are considered relatively safe because only low concentrations are transferred into breast milk.

Rho-Kinase (ROCK) Inhibitors

Netarsudil, approved by the FDA and EMA, is highly protein-bound with minimal systemic absorption.

Table 1: Summary of antiglaucoma medications during pregnancy and lactation

Drug class	*1st trimester*	*2nd Trimester*	*3rd Trimester*	*Lactation*
β-Blockers	Second-line	First-line	Second-line	First-line
Prostaglandin analogues	Third-line	Third-line	Avoid	First-line
Topical carbonic anhydrase inhibitors	Third-line	Third-line	Second-line	First-line
Brimonidine	Second-line	Second-line*	Avoid	Avoid
ROCK inhibitors	Avoid	Avoid	Avoid	Avoid

Legend

First-line – Preferred option when medical therapy is required.

Second-line – Use when first-line therapy is unsuitable or inadequate.

Third-line – Reserve for selected patients after individualized maternal–fetal risk assessment.

Avoid – Not recommended because of known/potential fetal or neonatal risks or insufficient safety data.

*If brimonidine is initiated early in pregnancy, transition to an alternative agent and discontinue before the late third trimester because of the risk of neonatal central nervous system depression and apnea.

Animal studies demonstrated embryo-fetal toxicity only at doses far exceeding therapeutic ophthalmic levels. While no clear teratogenicity has been observed at physiological doses, caution is advised during pregnancy and lactation due to limited human data. A summary of the antiglaucoma medications used during pregnancy and lactation is presented in Table 1.

Role of Laser Therapy

Selective laser trabeculoplasty (SLT) and argon laser trabeculoplasty (ALT) are considered safe and effective across all trimesters. Although the IOP-lowering effect may be temporary, laser therapy is useful for reducing medication burden during pregnancy and lactation.

Surgical Management

Surgery should be avoided whenever possible and reserved for refractory cases.

Timing and Positioning

When surgical intervention becomes necessary during pregnancy, it is preferably deferred until the second trimester whenever feasible. During surgery, prolonged supine positioning should be avoided to minimize the risk of aortocaval compression.

Anesthesia Considerations

Local anesthetics such as lidocaine and prilocaine are generally considered acceptable during pregnancy because available clinical experience has not demonstrated an increased risk of major congenital malformations when used at therapeutic doses. General anesthesia in the first trimester has been associated with low birth weight and neural tube defects. Sub-Tenon or topical anesthesia is favored over retrobulbar blocks.

Surgical Challenges

Glaucoma surgery during pregnancy presents several challenges, including an increased risk of thromboembolic events and tissue edema that may adversely affect wound healing. The use of antimetabolites such as mitomycin C and 5-fluorouracil should generally be avoided during pregnancy because of their antiproliferative effects and evidence of fetal toxicity from animal studies, unless the potential maternal benefit clearly outweighs the fetal risk. Alternative strategies include releasable sutures, collagen matrix implants (Ologen), and valved glaucoma drainage devices to optimize surgical outcomes while minimizing fetal exposure to potentially harmful agents.

Minimally invasive glaucoma surgery (MIGS) has emerged as a promising alternative for selected patients with mild-to-moderate glaucoma because it is associated with smaller incisions, reduced tissue manipulation, shorter operative times, and faster postoperative recovery compared with conventional filtration surgery. An additional advantage is that most MIGS procedures do not require the routine use of antimetabolites, which may be particularly beneficial during pregnancy. However, evidence regarding the safety and efficacy of MIGS in pregnant patients remains limited, with current recommendations largely extrapolated from studies in non-pregnant populations. Therefore, MIGS should be considered on an individualized basis in carefully selected patients when surgical intervention is necessary, and further studies are required before it can be routinely recommended during pregnancy.

Discussion

Successful management of glaucoma during pregnancy requires close collaboration between ophthalmologists and obstetricians. Laser therapy serves as an effective adjunct, while surgery remains a last resort. Patient counseling, frequent monitoring, and individualized risk-benefit assessment are essential.

Conclusion

Glaucoma management during pregnancy and lactation demands careful balancing of maternal visual needs and fetal safety. Trimester-based medication selection, minimization of systemic exposure, preference for laser therapy, and judicious surgical intervention form the cornerstone of care. Further prospective studies are required to establish definitive safety profiles, particularly for newer antiglaucoma agents.

Funding

No funding was received for this review article.

Conflict of Interest

The author declares no conflict of interest.

Author Declaration

The manuscript has been read and approved by the author and represents honest work. The manuscript is original, has not been published previously, and is not under consideration elsewhere.

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