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1 SUMMARY IN ENGLISH:

The aim of this study is to summarize the current knowledge on the management of glaucoma in pregnant and breastfeeding patients by reviewing and evaluating disease prevalence, pathogenetic basis, disease prevalence, diagnostic features and treatment challenges. A structured narrative literature review was conducted, primarily selecting high quality scientific articles mainly from the past 10 years from PubMed, ScienceDirect, and Google Scholar databases, as well as evidence-based guidelines such as the 6th edition of the European Glaucoma Society guidelines.

Glaucoma during pregnancy represents a complex clinical challenge that requires careful management to preserve maternal vision while minimizing risks to the developing fetus. Although many pregnant women experience a physiological reduction in intraocular pressure (IOP) due to hormonal, circulatory, and biomechanical changes, this effect is variable and cannot be relied upon to protect all patients, particularly those with pre-existing glaucoma. Risk factors such as age, ethnicity, family history, ocular anatomy, and systemic conditions may influence disease progression and require careful assessment before and during pregnancy.

Monitoring glaucoma during pregnancy can be challenging. Physiological changes in the cornea may affect IOP measurements, and visual field testing can be less reliable due to fatigue or discomfort. Imaging tools such as optical coherence tomography (OCT) and fundus photography are safe and valuable for assessing the optic nerve and retinal structures, helping clinicians detect early progression.

Treatment must be individualized and cautious. Topical medications, including beta-blockers and alpha-2 adrenergic agonists, are generally preferred first line, while prostaglandin analogues and systemic carbonic anhydrase inhibitors should be reserved for cases where benefits clearly outweigh fetal risks. Non-pharmacological strategies, such as lifestyle modifications and structured monitoring, are important adjuncts. Laser procedures, including selective laser trabeculoplasty (SLT) and laser peripheral iridotomy (LPI), can reduce medication dependence and are considered safe during pregnancy. For patients with progressive or vision-threatening glaucoma, surgical options may be required. Minimally invasive glaucoma surgery (MIGS) and trabeculectomy, performed with careful anesthesia management and preferably in the second trimester, can provide effective IOP control while limiting fetal exposure. Postoperative care,

including the careful use of topical antibiotics, corticosteroids, and cycloplegic agents, is essential to maintain safety.

Postpartum monitoring is critical, as sudden hormonal changes can cause rebound increases in IOP, requiring adjustment of medications during lactation. Overall, the management of glaucoma in pregnant and breastfeeding women requires a personalized, multidisciplinary, and evidence-based approach. Despite advances in diagnostics, medications, and surgical techniques, further research is needed to ensure optimal outcomes for both mother and child.

Keywords: Glaucoma; Pregnancy; Lactation; Postpartum, Intraocular pressure; Antiglaucoma medications, medical glaucoma treatment, glaucoma surgery

2 SUMMARY IN LITHUANIAN:

Šio tyrimo tikslas yra apibendrinti dabartines žinias apie nėščiųjų ir krūtimi maitinančių pacienčių glaukomos priežiūrą apžvelgiant ir įvertinant ligos paplitimą, patogenezinį pagrindą, diagnostikos ypatumus ir gydymo iššūkius. Atlikta struktūruota naratyvinė literatūros apžvalga atrenkant pagrįste daugiausia per paskutiniųjų 10 m. Aukštos kokybės PubMed, ScienceDirect, Google Scholar duomenų bazių mokslinius straipsnius bei vadovaujantis įrodymais pagrįstomis rekomendacijomis, tokiomis kaip Europos glaukomos draugijos 6-osios redakcijos gairės.

Glaukoma nėštumo metu yra sudėtingas klinikinis uždavinys, reikalaujantis kruopštaus gydymo, siekiant išsaugoti motinos regėjimą ir kartu kuo labiau sumažinti riziką besivystančiam vaisiui. Nors daugeliui nėščių moterų dėl hormoninių, kraujotakos ir biomechaninių pokyčių akispūdis fiziologiškai sumažėja, šis reiškinys yra nevienodas ir negalima pasikliauti, kad jis apsaugos visas pacientės, ypač tas, kurios jau serga glaukoma. Tokie rizikos veiksniai kaip amžius, etninė priklausomybė, šeimos istorija, akies anatomija ir sisteminės ligos gali turėti įtakos ligos progresavimui, todėl prieš nėštumą ir jo metu būtina atlikti atidų vertinimą.

Glaukomos stebėjimas nėštumo metu gali būti sudėtingas. Fiziologiniai ragenos pokyčiai gali turėti įtakos VAK matavimams, o regos lauko tyrimai gali būti mažiau patikimi dėl nuovargio ar diskomforto. Vaizdo gavimo priemonės, tokios kaip optinė koherentinė tomografija (OCT) ir akies dugno fotografavimas, yra saugios ir vertingos vertinant regos nervą ir tinklainės struktūras, padėdamos gydytojams anksti nustatyti ligos progresavimą.

Gydymas turi būti individualus ir atsargus. Paprastai pirmiausia teikiama pirmenybė vietiniams vaistams, įskaitant beta adrenoblokatorius ir alfa-2 adrenoreceptorių agonistus, o prostaglandinų analogai ir sisteminiai anglies dioksido anhidrazės inhibitoriai turėtų būti skiriami tik tais atvejais, kai nauda aiškiai viršija riziką vaisiui. Nefarmakologinės strategijos, tokios kaip gyvenimo būdo pokyčiai ir struktūriškai organizuota stebėseną, yra svarbūs pagalbiniai metodai. Lazerinės procedūros, įskaitant selektyvią lazerinę trabekuloplastiką (SLT) ir lazerinę periferinę iridotomiją (LPI), gali sumažinti priklausomybę nuo vaistų ir yra laikomos saugiomis nėštumo metu.

Pacientėms, sergančioms progresuojančia arba regėjimui pavojinga glaukoma, gali prireikti chirurginio gydymo. Mažai invazinė glaukomos chirurgija (MIGS) ir trabekulektomija, atliekamos taikant atsargų anestezijos valdymą ir pageidautina antrajame nėštumo trimestre, gali užtikrinti veiksmingą VAK kontrolę, tuo pačiu ribojant vaisiaus ekspoziciją. Pooperacinė priežiūra, įskaitant atsargų vietinių antibiotikų, kortikosteroidų ir ciklopeginių vaistų vartojimą, yra būtina saugumui užtikrinti.

Stebėjimas po gimdymo yra ypač svarbus, nes staigūs hormoniniai pokyčiai gali sukelti akispūdžio atšokamąjį padidėjimą, dėl kurio žindymo laikotarpiu tenka koreguoti vaistų dozes. Apskritai, glaukomos gydymas nėščioms ir žindančioms moterims reikalauja individualizuoto, daugiadisciplinio ir įrodymais pagrįsto požiūrio. Nepaisant pažangos diagnostikos, vaistų ir chirurginių metodų srityse, reikalingi tolesni moksliniai tyrimai, siekiant užtikrinti optimalius rezultatus tiek motinai, tiek vaikui.

Raktažodžiai: glaucoma, nėštumas, žindymo laikotarpis, akispūdis, vaistai nuo glaukomos, laikotarpis po gimdymo, medicininis glaukomos gydymas.

ABBREVIATIONS:

BAK – Benzalkonium Chloride
CAI – Carbonic Anhydrase Inhibitor
CCT– Central Corneal Thickness
CSF – Cerebrospinal Fluid
FDA – Food and Drug Administration
GATT – Gonioscopy-Assisted Transluminal Trabeculotomy
IOP – Intraocular Pressure
LBW– Low birth weight
LPI – Laser Peripheral Iridotomy
MIGS – Minimally Invasive Glaucoma Surgery
Nd: YAG – neodymium–yttrium–aluminium–garnet
NICU–neonatal intensive care unit
NTG – Normal-Tension Glaucoma
OCT – Optical Coherence Tomography
PACD – Primary Angle-Closure Disease
PACG – Primary Angle-Closure Glaucoma
POAG – Primary Open-Angle Glaucoma
RNFL – Retinal Nerve Fiber Layer
SLT – Selective Laser Trabeculoplast

3 INTRODUCTION

Glaucoma is a chronic and progressive optic neuropathy marked by the loss of retinal ganglion cells and corresponding visual field defects. It remains one of the leading causes of irreversible blindness worldwide (1). Rather than a single disease, it represents a group of conditions with different causes, clinical presentations, and treatment approaches, all of which require accurate diagnosis and long-term follow up (2). Among its main subtypes, primary angle closure glaucoma is particularly important due to its anatomical basis and its potential to cause both acute and chronic increases in IOP (3). In addition to adult-onset disease, ocular health may also be influenced by systemic and obstetric factors, including those related to cesarean delivery (4), while congenital conditions such as primary congenital glaucoma contribute to early onset disease (5). The pathophysiology of glaucoma is complex and not fully understood. Both IOP-dependent and IOP-independent mechanisms are involved, including vascular factors and hormonal influences (6). Pregnancy introduces significant physiological changes that can affect the eye, including alterations in corneal thickness, ocular blood flow, and IOP (7). These changes are not uniform and may differ between individuals, reflecting the interaction between normal adaptation and underlying disease processes (8). As a result, managing glaucoma during pregnancy requires careful consideration of both maternal and fetal factors (9), and remains a challenging and evolving area of clinical practice (10). Increasingly, an individualized and multidisciplinary approach is recommended, particularly during pregnancy and breastfeeding (11,12). One of the main concerns in this setting is the safety of antiglaucoma medications. Many commonly used drugs can cross the placenta or be excreted in breast milk, raising concerns about potential effects on the fetus or newborn (13,14). While medical therapy is usually the first-line approach, alternative options such as MIGS or other surgical techniques may be needed when medications are insufficient (15,16). However, surgery during pregnancy requires careful planning, including consideration of anesthesia and perioperative risks (17). There is also growing evidence that hormonal and reproductive factors may influence glaucoma risk and progression in women (18). This has led to increased interest in sex-specific aspects of the disease, particularly in relation to pregnancy and hormonal changes (19). From a public health perspective, glaucoma continues to represent a significant global burden, including in the context of pregnancy and postpartum care (20). Management strategies therefore need to

consider both ocular and systemic factors (21), including the possible role of estrogen in disease modulation (22). Pregnancy may also be associated with other ocular conditions, such as inflammatory or chorioretinal disorders, which can complicate both diagnosis and management (23). Systemic diseases like diabetes may further increase the risk of glaucoma or affect its course (24). As the global burden of glaucoma continues to rise, early detection and effective treatment remain essential (25). Advances in surgical techniques have broadened available treatment options (26), including in complex cases such as those involving corneal transplantation (27) or vitreoretinal surgery (28). At the same time, sex-specific differences in eye disease are gaining more attention, highlighting the need to better understand glaucoma in women (29). In some cases, surgical procedures such as trabeculectomy may be required during pregnancy, although available evidence is still limited (30). Other considerations include the use of intravitreal therapies and their potential effects in this population (31). Changes in IOP in the perioperative period can further complicate management (32), requiring careful assessment of risks and benefits in each case (33). Environmental and lifestyle factors, including smoking, may also play a role in disease progression (34), and neuro-ophthalmic issues may occasionally arise in the context of pregnancy (35). Reproductive factors have increasingly been linked to glaucoma and related traits, suggesting a complex interaction between hormonal exposure and disease risk (36). In addition, lifestyle and systemic factors such as diet, sleep, and blood pressure may influence disease progression (37). Certain medications, including brimonidine, have been studied for their safety in sensitive populations (38). Importantly, disease progression has been reported in some patients after discontinuation of treatment during pregnancy, particularly in the postpartum period (39). Although understanding of glaucoma continues to improve, many aspects of its pathophysiology and management remain under investigation (40). Clinical recommendations emphasize the importance of risk assessment and individualized treatment planning during pregnancy (41,42). International guidelines provide a framework for diagnosis and management, including surgical approaches such as trabeculectomy (42–44). Epidemiological studies have identified key risk factors and patterns of disease distribution, including age-related trends and the high proportion of undiagnosed cases (45,46). Screening and early detection are therefore essential, especially in populations at increased risk of angle-closure glaucoma (42,47,48). With global prevalence expected to rise further, there is a growing need for improved strategies targeting vulnerable groups (49). Pregnancy itself is associated with a range of ocular changes, most of which are temporary but may still affect pre-existing conditions (50). Surgical and anesthetic interventions during this period require

careful evaluation because of potential risks to both mother and fetus (51). Clinical guidelines continue to evolve as new evidence emerges (52). At the same time, the systemic effects of topical glaucoma medications must be considered (53), along with variability in clinical practice (54). Observational studies have explored possible links between glaucoma medications and neonatal outcomes (55), as well as real-world pregnancy outcomes in treated patients (56,57). Recent studies highlight the importance of individualized care and close monitoring throughout pregnancy and the postpartum period (58). In selected cases, laser therapies may help reduce the need for medications (59,60). Despite growing research in this area, important gaps remain in the evidence guiding glaucoma management during pregnancy. This work aims to summarize current knowledge on glaucoma in pregnant and breastfeeding women, including its prevalence, pathophysiology, diagnosis, and management. By bringing together perspectives from ophthalmology, obstetrics, and pharmacology, it seeks to support clinical decision making and promote individualized care. In addition, it evaluates the safety and effectiveness of available treatments, addresses diagnostic and therapeutic challenges, identifies gaps in current knowledge, and outlines priorities for future research, with the overall goal of improving outcomes for both mother and child.

4 Purpose and aims

The purpose of this study is to provide a comprehensive synthesis of current knowledge on glaucoma in pregnant and breastfeeding women.

The study aims to:

- 1) overview and evaluate the evidence of its prevalence and pathophysiological mechanisms.
- 2) to explore and assess the diagnostic and therapeutic approaches.
- 3) to evaluate the safety and effectiveness of medical, laser, and surgical treatment options and the management strategies.
- 4) to support evidence based clinical decision-making and individualized patient care during pregnancy and lactation.
- 5) to identifies the gaps in current knowledge, and highlight priorities for future research, with the goal of improving outcomes for both mother and child.

5 METHODOLOGY:

5.1 Data Sources

This thesis is based on a structured narrative literature review aimed at identifying high-quality scientific evidence related to glaucoma during pregnancy and lactation. The literature search was conducted using three major biomedical databases: PubMed, ScienceDirect, and Google Scholar, selected for their broad coverage of peer-reviewed clinical and ophthalmologic research. Additional relevant publications were identified through reference lists of key articles.

The review focused on publications mainly from the last ten years to ensure that the findings reflect the most current knowledge but even earlier than 10 years sources was also used to support the thesis. Although English language publications were prioritized, relevant studies published in other languages including Spanish, Swedish, German, and Polish were translated into English and included to ensure a comprehensive review. Only articles presenting results of studies in humans were included.

5.2 Search Strategy

The literature search was conducted using a systematic strategy based on predefined keywords and combinations of relevant medical subject terms. Search terms were applied individually and in combination to refine results and capture variations in terminology.

The search terms included:

“Glaucoma and/or/in pregnancy and management”, “pregnancy and intraocular pressure”, “glaucoma medications and/in pregnancy”, “glaucoma medications and/in breastfeeding”, “glaucoma surgery and pregnancy”.

Boolean operators (and, or, in) were used to combine search terms, and filters were applied for publication date, language, and article type to ensure the inclusion of clinically relevant and methodologically sound studies.

5.3 Study Selection and Screening Process

After retrieving all potentially relevant publications, duplicate records were removed. The remaining articles underwent a two-stage screening process. First finding all possible sources within the last decade and then including only the once that is mainly relevant to the thesis.

Title and Abstract Screening

Titles and abstracts were reviewed to assess relevance to the topic of glaucoma during pregnancy. Articles were included if they addressed areas of:

- glaucoma management during pregnancy
- ocular physiological and pathophysiological changes during gestation
- diagnostic challenges during pregnancy
- antiglaucoma medication safety during pregnancy and breastfeeding
- surgical glaucoma treatment options during pregnancy
- postpartum and lactation considerations in glaucoma patients

5.4 Full-Text Review

Articles that met the first stage screening criteria were evaluated in full to confirm their scientific quality, relevance, and applicability to clinical practice.

Selected studies were categorized according to their primary theme, including:

- Physiological effects of pregnancy on intraocular pressure.
- Diagnostic methods -Medication safety.
- Laser and surgical management.
- Postpartum and lactation considerations.

This thematic categorization supported the structured integration of evidence throughout the thesis.

Inclusion Criteria for content

Studies were included if they met at least the following criteria:

- Addressed glaucoma during pregnancy, the postpartum period, or lactation.
- Investigated the effects of pregnancy on ocular physiology, particularly intraocular pressure (IOP), corneal biomechanics, or vascular changes.
- Evaluated the diagnostic accuracy of tonometry, visual field testing, or ocular imaging during pregnancy.
- Assessed the safety or effectiveness of antiglaucoma medications in pregnant or breastfeeding women.
- Examined laser therapy or surgical approaches to glaucoma management during pregnancy, including trabeculectomy, tubecoplasty, minimally invasive glaucoma surgery (MIGS), or other relevant procedures.

- Described hormonal or systemic factors that may influence glaucoma risk Presented expert guidelines, clinical case series, or review articles relevant to the management of glaucoma in pregnant patients.

Exclusion Criteria for content

Articles were excluded if they met one of the following conditions:

- Were outdated and replaced by more recent or higher quality evidence.
- Demonstrated weak methodology or insufficient supporting data.
- Consisted primarily of opinion-based content lacking scientific evidence.
- Included women outside the reproductive age range, such as postmenopausal participants, unless directly relevant to pregnancy related glaucoma.
- Did not provide evidence supporting the specific topics addressed in the review.

5.5 Types of Studies Included

Because glaucoma during pregnancy is relatively uncommon, large prospective clinical trials are limited. Therefore, a range of study designs was included to provide a comprehensive overview of available evidence.

The types of publications included:

- Narrative and systematic reviews
- Articles and published readings
- Clinical guidelines.
- Clinical studies and questionnaire survey.
- Population-based-case-control studies
- Multicenter descriptive study
- Retrospective cohort study
- Tertiary sources online medical reference sources

5.6 Data Extraction and Analysis

A qualitative synthesis approach was used to integrate findings from the selected studies.

Relevant data were extracted and organized into thematic categories, including:

- Physiological changes during pregnancy and their effects on intraocular pressure (IOP)
- Safety profiles of glaucoma medications

- Diagnostic challenges during pregnancy
- Laser and surgical treatment considerations
- Postpartum and breastfeeding implications
- Medication safety was evaluated using available pharmacological evidence, regulatory recommendations, and teratology resources, supporting clinically relevant recommendations.

5.7 Use of Artificial Intelligence Tools

Artificial intelligence-based tools were used in a limited and supportive capacity during the preparation of this thesis. These tools assisted with text organization, language clarity, and stylistic refinement of sections drafted by the author.

All scientific content, literature interpretation, analysis, and conclusions represent the independent work of the author. AI tools were not used to generate original data, perform analysis, or create references. All sources included in this thesis were independently selected, verified, and cited by the author.

5.8 Summary of Literature Review Results

After applying the predefined eligibility criteria, 44 references were selected as the final body of evidence for this thesis. To support the results of the review, studies cited within these sources were also used and acknowledged. References numbered 45 onward in the reference list correspond to the original studies cited by the included sources and other recommended studies from the supervisor that was relevant to the thesis and were included to accurately represent and credit the evidence presented in the selected studies due to the limited sources in the last decade some sources was used even if they were not exactly within the last decade but these sources was still included to support the thesis and make it more scientifically based.

6 RESULTS

6.1 Epidemiology

Glaucoma is traditionally considered an age-related disease, affecting approximately 2–3% of individuals over the age of 40 (45), with prevalence increasing significantly as age advances. However, its occurrence in younger populations particularly among women of reproductive age remains less well understood. This gap in knowledge is largely since most population-based studies focus on older age groups.

Nevertheless, available evidence suggests that glaucoma is not exclusively a disease of later life. For instance, a population-based study conducted in Japan reported measurable rates of open-angle glaucoma among younger women, with a prevalence of 0.48% in those aged 15–24 years, 0.42% in the 25–34 age group, and 0.73% in women aged 35–44 years (45).

Although these figures are lower than those observed in older populations, they indicate that a meaningful proportion of younger women may already be affected by the disease.

In clinical practice, it is not uncommon to encounter women in the reproductive age group who developed glaucoma earlier in life due to conditions such as congenital glaucoma, anterior segment dysgenesis, or glaucoma following pediatric cataract surgery. These disorders often result in chronic optic nerve damage well before adulthood. Additionally, women of reproductive age may be affected by various forms of secondary glaucoma (20,33,45).

6.2 Glaucoma Classification, Anatomy and Pathophysiology

6.2.1 Classification of Glaucoma

Glaucoma comprises a heterogeneous group of optic neuropathies characterized by progressive loss of retinal ganglion cells, structural damage to the optic nerve head, and corresponding visual field defects (1,2). Clinically, glaucoma is classified anatomically into open-angle and angle-closure forms, and etiologically into primary or secondary types (1,2,3,32,40,42).

Primary glaucoma occurs in the absence of an identifiable secondary cause and is traditionally divided into:

Primary open-angle glaucoma (POAG) characterized by an open anterior chamber angle ($\geq 180^\circ$ of posterior trabecular meshwork visible), no peripheral anterior synechiae,

progressive optic nerve damage, and visual field loss. Untreated IOP usually exceeds 21 mmHg (1,2,32,40,42).

Normal-tension glaucoma (NTG) glaucomatous optic neuropathy occurs despite normal IOP. Vascular dysregulation and reduced optic nerve perfusion contribute to progression, and hormonal factors such as fluctuations in estrogen and progesterone may influence disease course (11,32,40,42).

Primary angle-closure glaucoma (PACG) caused by closure of the anterior chamber angle due to pupillary block, plateau iris, or lens-related crowding. Gonioscopy shows nonvisible posterior trabecular meshwork ($\geq 180^\circ$) and peripheral anterior synechiae, with glaucomatous optic neuropathy (1,2,3,32,40,42).

From a clinical and epidemiological perspective, the glaucoma types most likely to be encountered in women of reproductive age and during pregnancy are those more common in younger individuals, rather than age-related primary open-angle glaucoma. These include congenital and juvenile glaucoma, pigmentary glaucoma, uveitis glaucoma, traumatic glaucoma, and neovascular glaucoma, the latter often associated with systemic conditions such as diabetes mellitus type 2. This distribution is important when interpreting glaucoma in pregnancy, as many affected patients are more likely to have pre-existing or secondary disease rather than newly developed primary open-angle glaucoma.

Secondary glaucoma result from identifiable ocular or systemic conditions that disrupt aqueous humor dynamics, including post-surgical, trauma-related, or medication induced glaucoma (1,2,32,40,42). Additional important secondary forms include pseudo exfoliation glaucoma, uveitis glaucoma, and neovascular glaucoma secondary to retinal ischemic disease such as diabetic retinopathy or retinal vein occlusion, all of which are more frequently seen in younger or systemically affected patients.

Congenital and developmental glaucoma involve anterior segment abnormalities present from birth or early childhood. Primary congenital glaucoma arises from maldevelopment of the trabecular meshwork and Schlemm's canal, presenting in infancy (1,2,3,32,42). Juvenile open-angle glaucoma represents a later-onset developmental form that can present in adolescence or early adulthood and often has a stronger genetic component.

6.2.2 Glaucoma Anatomy:

Anterior Segment Anatomy and Aqueous Humor Dynamics

Aqueous humor dynamics play a key role in maintaining IOP and depend on a balance between fluid production and outflow. Aqueous humor is produced by the non-pigmented epithelium of the ciliary processes in the ciliary body. Its formation involves active secretion, ultrafiltration, and diffusion, with active ion transport particularly sodium and bicarbonate being the main driving mechanism. Carbonic anhydrase is essential in this process, as it supports bicarbonate formation and promotes osmotic fluid movement into the posterior chamber (1,3,40,42).

From the posterior chamber, aqueous humor flows through the pupil into the anterior chamber. In addition to regulating IOP, it provides nutrients and removes waste products from avascular structures such as the cornea and lens (1,3,40,42).

Aqueous humor exits the eye through two main pathways: the conventional (trabecular) and the uveoscleral pathways. The trabecular pathway is the primary route, where fluid passes through the trabecular meshwork at the iridocorneal angle, enters Schlemm's canal, and then drains into the episcleral venous system. The juxtacanalicular region of the trabecular meshwork offers the greatest resistance to outflow and plays a major role in determining IOP (1,2,32,40).

The uveoscleral pathway provides an additional route for outflow. Fluid moves between the ciliary muscle fibers into the suprachoroidal space, where it is absorbed by the sclera and surrounding vasculature. Although this pathway contributes less under normal conditions, it remains important in overall IOP regulation. Its activity is influenced by the extracellular matrix of the ciliary muscle and can be modified by hormonal and pharmacological factors (1,3).

Optic Nerve Head and Retinal Ganglion Cells

The optic nerve head, particularly the lamina cribrosa, is the main site of glaucomatous damage. Elevated IOP and reduced ocular perfusion led to loss of retinal ganglion cell axons, resulting in optic disc cupping and thinning of the retinal nerve fiber layer (1,32,40).

Systemic changes during pregnancy, such as increased blood volume, reduced vascular resistance, and higher levels of estrogen and progesterone, can temporarily influence optic nerve perfusion. These changes may mask subtle disease progression or increase susceptibility in eyes that are already at risk (11,12).

6.2.3 Glaucoma Pathophysiology:

Primary Open-Angle Glaucoma:

Although the exact cause of glaucoma remains unclear, elevated IOP is strongly associated with retinal ganglion cell loss and progressive optic nerve damage. IOP is determined by the balance between aqueous humor production in the ciliary body and its outflow through two main pathways: the trabecular meshwork (conventional) and the uveoscleral pathway (non-conventional). In POAG, increased resistance within the trabecular meshwork leads to reduced outflow and elevated IOP.

Glaucomatous optic neuropathy can also develop in individuals with normal IOP, known as NTG. One proposed mechanism is relatively low CSF pressure in the subarachnoid space surrounding the optic nerve, which may increase the pressure gradient across the lamina cribrosa and contribute to nerve damage. Vascular dysregulation also plays an important role, reflecting the impaired ability of ocular blood vessels to maintain stable perfusion despite changes in systemic blood pressure or metabolic demand. This can lead to inconsistent or reduced blood supply to the optic nerve head.

Repeated episodes of hypoperfusion, driven by autoregulatory failure, endothelial dysfunction, or increased vasoreactivity, may result in ischemia–reperfusion injury. This process promotes oxidative stress, mitochondrial dysfunction, and ultimately retinal ganglion cell death. Systemic factors such as nocturnal hypotension may further worsen ocular perfusion, increasing the risk of ongoing ischemic stress at the optic nerve (6,21,40).

Additional mechanisms implicated in glaucoma include impaired microcirculation, immune-related processes, excitotoxic damage, and increased oxidative stress. These factors may contribute to retinal ganglion cell injury even when IOP is within normal range. Moreover, primary neuronal damage can lead to secondary neurodegeneration affecting other retinal

neurons and structures along the central visual pathway, increasing overall vulnerability to disease progression (40).

Primary Angle-Closure Glaucoma:

PACG differs from POAG mainly in the anatomy of the anterior chamber angle, which determines aqueous humor outflow. In PACG, obstruction occurs when the peripheral iris meets the trabecular meshwork, reducing or blocking outflow.

Clinically, angle closure is identified by the absence of visible posterior trabecular meshwork on gonioscopy. Primary angle closure is typically defined as $\geq 180^\circ$ of iridocorneal angle closure, while more extensive involvement (usually $\geq 270^\circ$) is associated with more advanced disease. This corresponds to grading systems in which $\geq 180^\circ$ of visible trabecular meshwork indicates an open angle, while reduced visibility suggests progressive narrowing or closure (3,42).

Like POAG, PACG may be asymptomatic in early stages, with gradual narrowing of the anterior chamber angle. This reflects a progressive reduction in aqueous outflow due to increasing iridotrabecular contact, often related to anatomical predisposition such as a shallow anterior chamber or relative pupillary block.

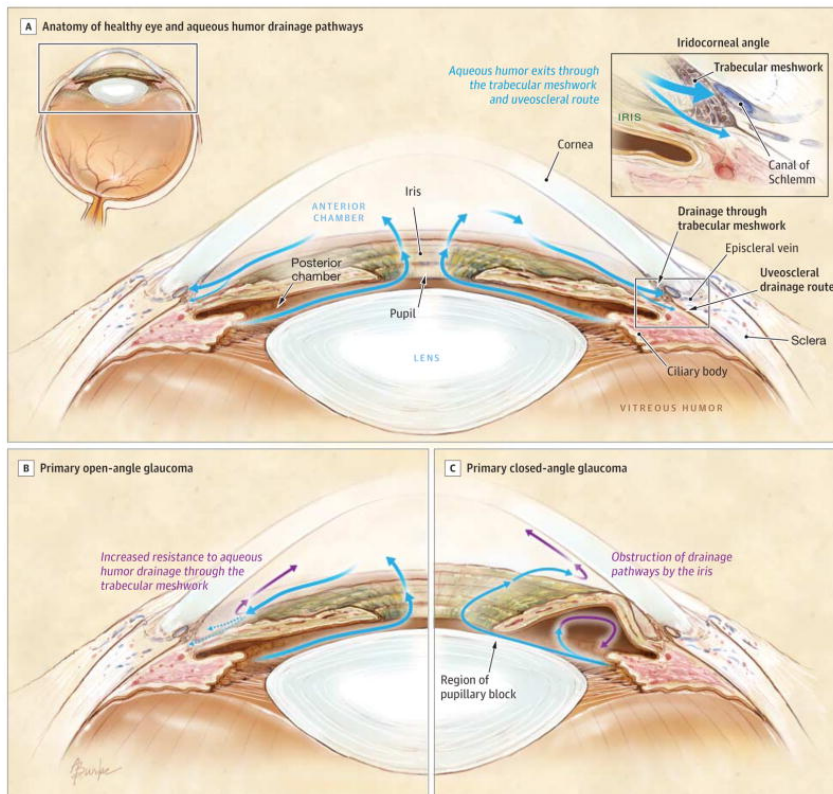
In susceptible individuals, this process can suddenly worsen, leading to complete angle closure. This results in a rapid rise in IOP due to abrupt cessation of trabecular outflow. The pressure increase is caused by impaired drainage rather than increased production and underlies acute angle-closure events (3,42).

PACG is primarily associated with anatomical features that predispose to a narrow or crowded anterior chamber angle, particularly involving the iris, lens, and ciliary body. Outflow is impaired due to appositional or synechial closure, preventing aqueous humor from reaching the trabecular meshwork and leading to a rapid increase in IOP (40).

The most common mechanism is pupillary block, where aqueous humor flow between the posterior and anterior chambers is restricted at the level of the pupil. This increases posterior chamber pressure, causing anterior bowing of the peripheral iris (iris bombe), which progressively narrows and may eventually close the angle.

Non-pupillary block mechanisms may also contribute. In plateau iris configuration, anteriorly positioned ciliary processes maintain a narrow angle despite a relatively normal central anterior chamber depth. Additional dynamic factors, such as pupillary dilation or choroidal expansion, can further reduce angle width by crowding the peripheral iris or shifting the lens–iris diaphragm forward. These mechanisms may act alone or in combination in the development of PACG (40,42).

Figure 1. Aqueous Humor Dynamics in Healthy and Glaucomatous Eyes (40).



6.3 Risk Factors for Glaucoma

Several risk factors for glaucoma are well established, with age and IOP remaining the strongest predictors of disease onset and progression (2,16,42,46). Other recognized risk factors for POAG include non-White ethnicity particularly Black ancestry family history, pseudo exfoliation, optic disc hemorrhage, thinner central corneal thickness, and myopia, all of which are associated with a higher risk of development and progression (2,16,42,46). PACG is most prevalent in East Asian populations, especially among individuals of Chinese descent (42,48).

Key anatomical risk factors for PACG include shallow anterior chamber depth, short axial length, increased lens thickness, anterior positioning of the lens iris diaphragm, and plateau iris configuration, all of which contribute to angle crowding and narrowing (42).

Additional ocular and systemic factors continue to be investigated to improve risk assessment. Corneal biomechanical properties have gained attention in recent years, although their exact role in glaucoma risk remains unclear (42). Systemic conditions such as diabetes and obstructive sleep apnea have shown inconsistent associations, highlighting the complex nature of glaucoma pathophysiology (42,47).

Blood pressure also appears to play an important role. Several studies suggest that low diastolic blood pressure is associated with an increased risk of glaucoma. Some evidence indicates that antihypertensive treatment, particularly when combined with low diastolic pressure, may further increase susceptibility of the optic nerve (42,47).

6.4 IOP in Pregnancy

Assessment of IOP during pregnancy necessitates an understanding of both standard reference values and the physiological changes that occur throughout the pregnancy. In the general adult population, normal IOP ranges from 10 to 21 mmHg, with values over this range raising concerns about ocular hypertension or glaucoma (32,33).

Pregnancy causes hormonal, vascular, and biomechanical changes that can affect both real IOP and the accuracy of measurement. As a result, interpreting IOP values in pregnant women becomes more difficult, necessitating critical clinical judgment rather than relying solely on established criteria (32,33).

Studies on ocular alterations in pregnancy, which examine IOP variations in hospitalized patients, show that glaucoma control is influenced not only by biological variables, but also by behavioral and environmental situations. According to research on pregnant women, IOP often decreases, particularly in the third trimester (50), owing primarily to hormonal changes. However, when researchers focused on women with preexisting glaucoma, the results were far less predictable. A retrospective case series discovered that slightly more than half of eyes were stable in terms of both IOP and visual fields, whereas nearly one in five had increased IOP and another one in five exhibited progressions of visual field loss despite stable or higher pressure (53). Although none of these individuals required surgery, others needed additional medical care. These findings clearly suggest that pregnancy does not consistently protect against glaucoma progression, and that close monitoring is still required (33,53).

A separate retrospective study looked at IOP changes in the non-operated eyes of patients hospitalized for unilateral glaucoma surgery (32). Only patients who were already taking glaucoma drugs saw a significant reduction in IOP following hospitalization, particularly those who were older or had a higher baseline IOP. The most likely explanation was increased adherence, as nurses observed or dispensed eye drops during hospitalization. Other contributory factors could have been psychological stress, changes in posture, and changes in systemic drugs. Interestingly, extended hospital stays were occasionally linked with increased IOP, probably due to stress or medication-related impacts (32).

These studies show that IOP is influenced not just by hormonal and physiological factors, but also by treatment adherence and the clinical setting. This emphasizes the necessity of customized interpretation of IOP readings and close, ongoing follow-up in pregnant women and glaucoma patients in general (32,33,50).

6.4.1 Physiological Lowering of IOP in Pregnancy

Most healthy pregnant women experience a moderate but constant reduction in IOP, often around 2-3 mmHg lower than pre-pregnancy values, especially in the second and third trimesters (7,8,10,21,32,33). This decline typically begins around mid-pregnancy, reaching a peak of 1-4 mmHg in the third trimester, and returns to baseline postpartum. In addition, diurnal IOP changes are frequently minimized during pregnancy.

This lowering in IOP is mostly caused by hormonal and vascular processes. Estrogens cause arterial and venous vasodilation, which lowers episcleral venous pressure, improves ocular perfusion, and increases aqueous humor outflow, all while contributing to optic nerve protection. Progesterone promotes aqueous outflow by reducing corticosteroid-induced resistance in the trabecular meshwork. Relaxin stimulates collagen remodeling by improving the permeability of the trabecular meshwork and sclera, which improves both trabecular and uveoscleral outflow. β -human chorionic gonadotropin (hCG) inhibits aqueous humor generation through cyclic AMP-mediated pathways in the ciliary body. Additional systemic variables, such as mild metabolic acidosis and widespread vasodilation, help to reduce aqueous production and enhance outflow (6,7,10,11,22).

These physiological modifications increase ocular blood flow while decreasing mechanical stress on the optic nerve (6,7,8). However, pregnancy-related corneal edema and increased corneal deformability may result in an underestimate of IOP, especially when evaluated using applanation-based procedures Tabel 1 (11).

Aside from IOP alterations, pregnancy is associated with several additional physiological ocular changes, including dry eye, decreased corneal sensitivity, mild corneal edema with increased thickness, decreased corneal stiffness, and increased ocular blood flow. While most of these changes are benign and reversible, pathological conditions such as progression of pre-existing diseases (glaucoma, diabetic retinopathy), new onset disorders (central serous chorioretinopathy), and ocular manifestations of systemic pregnancy-related diseases (preeclampsia) may occur, resulting in retinal, vascular, or optic nerve complications. IOP values within the normal adult range may nonetheless imply a relative increase

compared to a woman's pregnancy baseline, emphasizing the significance of close clinical monitoring (1,2,42,11).

Tabel 1. Changes affecting intraocular pressure and optic nerve during pregnancy (11).

Variables	Mechanisms	Results
> estrogens	> arterial vasodilation → systemic hypotension > arterial vasodilation → > ocular and cerebral blood flow	< aqueous production → IOP reduction Optic nerve protection against ischemic damage
	> venous vasodilation → < venous pressure > collagen synthesis → < lamina cribrosa deformability RGCs protection against IOP-related damage	> aqueous trabecular and uveo-scleral outflow → IOP reduction Optic nerve protection against mechanical damage Optic nerve neuroprotection
	> systemic water retention → corneal oedema	IOP underestimation
> relaxin	> collagen degradation → > corneal deformability	IOP underestimation
	> collagen degradation → > trabecular permeability	> aqueous trabecular outflow → IOP reduction
	> collagen degradation → > scleral permeability	> aqueous uveo-scleral outflow → IOP reduction
> progesterone	< effect of endogenous corticosteroids	> aqueous trabecular outflow → IOP reduction
> HCG	> cyclic adenosine monophosphate in the ciliary body	< aqueous production → IOP reduction
> metabolic acidosis	> arterial vasodilation → systemic hypotension	< aqueous production → IOP reduction
	> venous vasodilation → < venous pressure	> aqueous trabecular and uveo-scleral outflow → IOP reduction

6.4.2 Etiological influences of IOP Increase During Pregnancy

The causes of elevated IOP or glaucoma progression during pregnancy are multifactorial. Pre-existing structural changes, such as impaired trabecular meshwork function in POAG, plateau iris configuration, or congenital angle abnormalities, may limit the usual pregnancy-related reduction in IOP (1,2,3,7,10).

Secondary forms of glaucoma, including uveitic, pseudoexfoliative, and steroid-induced types, may also continue to cause IOP elevation despite the physiological changes of pregnancy (1,2,23,37). In addition, systemic conditions such as hypertension, preeclampsia, diabetes, and fluid retention can alter ocular hemodynamics and contribute to IOP variability during pregnancy (7,8,21,35).

Hormonal fluctuations, particularly in estrogen and progesterone levels, may further influence episcleral venous pressure and aqueous humor outflow, leading to changes in IOP and diurnal variation throughout pregnancy (6,7,11,22).

Sensitivity and Specificity of IOP Measurement in Pregnancy

Tonometry during pregnancy may be affected by corneal and biomechanical changes, which can reduce the accuracy and repeatability of IOP measurements. Pregnancy-related corneal thickening, increased hydration, and reduced corneal hysteresis may lead to variability in readings and a tendency to underestimate true IOP, thereby decreasing the sensitivity of tonometry for detecting mild pressure elevations. Observations from both the menstrual cycle and pregnancy suggest that sex hormones influence corneal properties, likely through receptors present in corneal tissue, although the exact molecular mechanisms remain unclear (7,8,10,30).

Diurnal IOP variation may also be more pronounced during pregnancy due to systemic fluid shifts and hormonal effects, reducing the reliability of single measurements (7,8). At the same time, the physiological decrease in IOP seen during pregnancy may mask early signs of glaucoma progression, particularly in patients with pre-existing optic nerve susceptibility (6,7,10).

6.4.3 Clinical Implications

Because IOP measurements are influenced by physiological changes during pregnancy, interpretation should be individualized (7,8,10,21). For instance, an IOP in the high teens may be acceptable for a healthy pregnant woman whose baseline is in the low teens, whereas the same value could be concerning in a patient with more advanced glaucoma. This highlights the importance of considering both target IOP and disease severity in clinical decision-making (33,40,42). Similarly, an apparent reduction in IOP may reflect hormonal and corneal biomechanical changes rather than true disease improvement, potentially masking progression if not interpreted in the correct clinical context (6,7,10,12).

Assessment of IOP during pregnancy therefore requires integration of standard reference values with individual baseline measurements, awareness of the multiple factors influencing IOP variability, and recognition of the limitations in sensitivity and specificity of routine tonometry and functional testing (1,2,7,10,12,21). This individualized approach is essential for identifying progression risk and guiding safe and effective glaucoma management throughout pregnancy (9,10,12,21,33).

6.5 General Principles of Glaucoma Diagnosis

Glaucoma diagnosis requires a detailed, multimodal assessment of structural and functional changes in the optic nerve and visual system. Since glaucoma often progresses silently in its early stages, establishing a reliable baseline before pregnancy is important for detecting any changes that may occur during gestation (7,10,42). Routine evaluation typically begins with IOP measurement, followed by optic nerve head examination, visual field testing, and assessment of the anterior chamber angle (2,40,41,42).

Although IOP is an important parameter, it cannot be used alone to diagnose glaucoma. Some patients develop glaucoma despite IOP values within the normal range (10–21 mmHg), while others with elevated IOP remain stable without progression. Therefore, IOP should always be interpreted alongside central corneal thickness, corneal biomechanics, and diurnal variation, all of which can influence measurement accuracy (32,33,42). During pregnancy, hormonal changes particularly increased progesterone may contribute to lower IOP through reduced episcleral venous pressure (6,7,8,10,42).

Structural assessment of the optic nerve head and RNFL is essential for diagnosis.

Stereoscopic ophthalmoscopy, fundus photography, and OCT can identify key features such as RNFL thinning, neuroretina rim loss, and increased cup-to-disc ratio. OCT provides objective and reproducible measurements and may detect structural damage before functional loss becomes apparent (41,42). Pregnancy-related vascular and hormonal changes may also influence optic nerve appearance, making baseline comparison particularly important (7,8,11,42).

Functional testing with automated perimetry remains essential for detecting typical visual field defects, including paracentral scotomas, arcuate defects, and nasal steps. Reliable interpretation requires repeat testing and consideration of factors such as fatigue, discomfort, and inexperience with the procedure (42).

Gonioscopy is used to evaluate the anterior chamber angle and determine the underlying glaucoma type and mechanism. Findings such as narrow or closed angles, plateau iris configuration, peripheral anterior synechiae, or congenital anomalies are important for guiding diagnosis and treatment. During pregnancy, fluid retention and anatomical changes may also influence anterior chamber configuration (42,43).

Modern glaucoma assessment also emphasizes risk stratification, including family history and systemic comorbidities. Since pregnancy can alter ocular physiology and IOP dynamics, a well-documented pre pregnancy baseline is essential for accurate interpretation of findings during gestation (33,42).

6.5.1 Screening and Early Detection

Early identification of glaucoma is particularly important in women of reproductive age (1,2). Screening typically includes IOP measurement, optic nerve assessment using ophthalmoscopy or OCT, and visual field testing to detect early functional changes (40,42). Women at higher risk such as those with a family history of glaucoma, congenital ocular abnormalities, or systemic conditions like diabetes or hypertension may benefit from closer and more frequent monitoring (9,24).

During pregnancy, screening should be adapted to ensure comfort and safety. Non-invasive methods are preferred, and prolonged supine positioning or stressful testing environments should be avoided when possible (7,8). Early detection of structural or functional changes allows for timely intervention, reducing the risk of irreversible optic nerve damage (11,12).

6.5.2 Diagnosis During Pregnancy

Assessing glaucoma during pregnancy requires careful adaptation of standard diagnostic methods to ensure both patient comfort and reliable evaluation. A multimodal approach combining structural, functional, and IOP assessment remains essential. However, physiological changes during pregnancy, including hormonal effects and altered ocular hemodynamics, may influence the interpretation of results.

No single diagnostic test is sufficient on its own; therefore, clinical assessment should be based on the combined interpretation of imaging, visual function testing, and IOP

measurements. Maintaining consistent follow-up and comparing findings with pre pregnancy baseline data are particularly important for distinguishing true disease progression from pregnancy related physiological changes.

An integrated patient centered approach helps maintain diagnostic accuracy while aligning with European Glaucoma Society recommendations (42).

Imaging Techniques Structural imaging, including optical coherence tomography OCT

OCT and fundus photography play an important role in glaucoma evaluation during pregnancy. Both methods are non-invasive and do not involve ionizing radiation, making them suitable for use in this population. OCT allows measurement of RNFL thickness and detailed assessment of the optic nerve head, enabling early detection of structural changes associated with glaucoma. Fundus photography provides serial documentation of optic nerve appearance over time, which is useful for monitoring potential progression. These techniques are most informative when combined with clinical examination and visual field testing (42). Interpretation of structural imaging during pregnancy requires caution due to hormonally mediated ocular changes. Variations in estrogen, progesterone, and relaxin levels can influence ocular blood flow, connective tissue properties, and fluid balance, potentially affecting RNFL measurements and optic nerve head appearance. As noted in recent studies, these changes may lead to subtle and temporary alterations that should not be misinterpreted as true disease progression (6,7,8,11).

Visual Field Testing

Automated perimetry remains essential for both the diagnosis and monitoring of glaucoma. Static automated perimetry provides quantitative assessment of visual function and supports detection of disease onset and progression. For reliable interpretation, testing conditions, devices, and parameters should be kept consistent across follow-up visits. Repeating tests when results are inconsistent or uncertain can improve confidence in identifying true progression.

Although structural imaging is valuable, visual field testing remains critical, particularly in early disease where structural changes may be subtle or not yet functionally evident.

Combining perimetry results with OCT findings and clinical examination improve overall diagnostic accuracy and supports better clinical decision making (42).

While hormonal changes do not directly affect visual field testing, pregnancy related systemic symptoms may indirectly influence test reliability. Fatigue, nausea, and reduced concentration can increase variability and reduce the consistency of perimetric results (7,8,11,42).

Tonometry Considerations

IOP measurement is a key component of glaucoma evaluation and follow-up. Accurate and consistent tonometry is essential, as IOP remains a major risk factor for disease progression. The European Glaucoma Society recommends using the same tonometer type and measurement technique at follow-up visits to ensure reliable trend analysis. CCT can influence IOP readings, with thicker corneas tending to overestimate and thinner corneas underestimating true pressure. However, the use of unvalidated CCT based correction formulas is not recommended. IOP should always be interpreted in the context of the overall clinical picture, including structural and functional findings. The most reliable assessment is achieved by integrating consistent tonometry with visual field testing and OCT imaging (42). During pregnancy, hormonal changes significantly influence IOP regulation. Increased levels of estrogen, progesterone, human chorionic gonadotropin, and relaxin contribute to lower IOP through enhanced aqueous outflow, reduced episcleral venous pressure, and decreased aqueous production. At the same time, pregnancy related fluid retention may lead to corneal edema and increased corneal thickness, potentially causing underestimation of IOP during measurement. These combined effects highlight the need for cautious interpretation of IOP in pregnant patients and reinforce the importance of comprehensive structural and functional assessment (6,7,8,10,11,42).

6.7 Glaucoma Management Across the Reproductive Period

6.7.1 Pre-Conception Considerations

Pre-conception counseling is crucial for women with glaucoma. Baseline IOP, optic nerve structure, and treatment regimens should be documented prior to pregnancy. Stabilizing IOP and optic nerve health before conception helps reduce the risk of disease progression during gestation. Systemic conditions such as hypertension and diabetes should be optimally managed, as they can influence ocular perfusion and IOP during pregnancy (20,33,42).

6.7.2 General Considerations of Glaucoma Management During Pregnancy

6.7.2.1 *First Trimester*

Rapid hormonal changes, particularly in estrogen and progesterone levels, can influence aqueous humor dynamics, ocular blood flow, and IOP (7,11,12,33,42). Since organogenesis may already be underway when pregnancy is first recognized, this period represents the highest fetal vulnerability. For this reason, an early and thorough discussion is essential regarding medication risks, IOP-lowering strategies, dose adjustments, reduction of systemic absorption, and the possibility of tapering or temporarily discontinuing treatment during pregnancy (34).

Management is primarily conservative, with close monitoring and preference for non-pharmacological approaches when possible. If medical treatment is necessary, brimonidine (category B) is generally considered the safest topical option. Other commonly used glaucoma medications, including β -blockers, prostaglandin analogues, and carbonic anhydrase inhibitors, should be avoided whenever possible due to potential fetal or pregnancy-related risks (7,11,12,33,34,42).

Glaucoma surgery is usually avoided during the first trimester, as anesthetic agents, sedatives, and antimetabolites may increase the risk of teratogenic effects and spontaneous abortion (34).

6.7.2.2 *Second Trimester*

In the second trimester, hormonal levels tend to stabilize, making IOP more predictable. This period is generally considered the safest window for procedures requiring prolonged positioning. Brimonidine may be used when clinically indicated, and topical β -blockers can also be considered, with appropriate monitoring of fetal heart rate and growth. Prostaglandin analogues should be used cautiously due to a potential risk of uterine contractions; patients should be advised about symptoms of preterm labor and instructed to discontinue the medication if such symptoms occur. Topical or oral carbonic anhydrase inhibitors may be used as adjunctive therapy, when necessary, with consideration of fetal growth monitoring during treatment.

If medical therapy needs adjustment or is insufficient, laser procedures such as SLT or LPI may be considered to reduce fetal exposure to medications. When IOP remains uncontrolled despite medical and laser therapy, surgical intervention may still be required. If surgery is necessary, the second trimester is generally preferred to minimize risks to both mother and fetus (20,33,34,42).

6.7.2.3 Third Trimester

In the third trimester, brimonidine, β -blockers, and topical carbonic anhydrase inhibitors may be used with caution when necessary. Prostaglandin analogues are generally avoided due to the potential risk of premature labor, particularly in early third trimester. Later in pregnancy, brimonidine should be discontinued because of the risk of neonatal central nervous system depression, making topical carbonic anhydrase inhibitors a more suitable option if treatment is required.

Laser procedures such as ALT or SLT may be used throughout pregnancy and can provide short-term IOP control, although their long-term effectiveness is limited. They may therefore serve as a bridge therapy until delivery.

Physiological changes in late pregnancy, including increased blood volume, fluid retention, and altered systemic vascular resistance, can still influence IOP and optic nerve perfusion. Labor may also cause transient increases in IOP, and cesarean delivery may be considered in selected cases of unstable glaucoma (4,20,33,42).

Glaucoma surgery in the third trimester is reserved for cases with strong clinical indications. When performed, careful consideration must be given to fetal risks associated with anesthesia, sedative agents, and antimetabolites (33).

6.7.3 Non-Pharmacological Approaches to Glaucoma Management During Pregnancy

Managing glaucoma during pregnancy requires a careful balance between preserving maternal vision and protecting fetal development. For many patients with mild or stable disease, non-pharmacological strategies form the basis of care. These focus on close

observation, structured follow-up, lifestyle measures, and patient education before initiating or escalating medical or surgical treatment (32,33,42).

Regular monitoring is central to this approach. Physiological changes during pregnancy can influence IOP, which may naturally decrease or fluctuate over time. Routine assessments, including IOP measurement, optic nerve evaluation, and visual field testing, allow for ongoing evaluation of disease status while minimizing risk. This approach helps identify true progression in a timely manner while avoiding unnecessary treatment in stable cases (32,33,42).

Lifestyle measures provide additional support for both ocular and systemic health. A balanced diet, adequate rest, and good sleep hygiene contribute to overall well-being. Careful management of systemic blood pressure is particularly important in pregnant patients with comorbid conditions. Smoking and exposure to secondhand smoke should be avoided, as they may negatively affect vascular function and ocular blood flow (34,37). Although simple, these measures can meaningfully support overall disease stability.

Patient counseling is equally important. Clear and empathetic communication regarding treatment goals, risks, and safe management options helps patients remain informed and engaged. Education also improves adherence to follow-up schedules and reinforces realistic expectations, where the primary goal during pregnancy is often to maintain stable vision while minimizing exposure to potentially harmful medications or procedures. Postpartum follow-up should also be discussed, as IOP and treatment needs may change after delivery (12,21,24,32).

These non-pharmacological strategies provide a low-risk, patient-centered framework for glaucoma management during pregnancy. When combined, careful monitoring, supportive lifestyle measures, and effective patient education help preserve maternal vision while minimizing fetal exposure and allowing safe transition to further treatment when needed (12,21,24,32,34,37).

6.7.4 Medical Management of Glaucoma in Pregnancy

Effective glaucoma management during pregnancy requires an individualized, stage-based approach that considers disease severity as well as the physiological changes of gestation.

Treatment decisions must balance preservation of maternal vision with fetal safety, with therapy adjusted according to both trimester and baseline disease status.

Anesthesia and surgical interventions carry risks for both mother and fetus. Glaucoma surgery is generally considered safest in the second trimester, as this reduces the risk of anesthesia related teratogenic effects and avoids the higher risk of miscarriage associated with first trimester procedures. Surgery in the third trimester is usually avoided due to practical and obstetric concerns, including maternal positioning difficulties, increased risk of preterm labor, fetal distress, and less favorable tissue handling and wound healing.

Pregnant patients may also have a higher risk of surgical failure due to younger age and the contraindication of antimetabolites such as mitomycin C. In such cases, trabeculectomy with an Ologen implant may be a safer alternative, as it allows modulation of wound healing without standard antimetabolites, helping to balance surgical effectiveness with fetal safety (33,42).

6.7.5 Anti-glaucoma Medicines

The main challenge in prescribing antiglaucoma medications during pregnancy is balancing effective IOP control with fetal safety. To date, no antiglaucoma drug has been proven completely safe for use during pregnancy (9,33,34,40,42).

Drug safety was classified by the U.S. Food and Drug Administration (FDA) using categories A, B, C, D, and X Table 2. These classifications were largely based on animal data and did not always reflect human outcomes Table 2 (52). Due to the lack of well-designed clinical trials in pregnant women, no antiglaucoma medication was ever placed in Category A. In general, Category B and C drugs were considered relatively safer, Category D drugs were avoided when possible, and Category X drugs were contraindicated due to known teratogenic risk (9,33,34,40,42).

This system has since been replaced. The FDA now requires detailed pregnancy and lactation labeling, providing narrative summaries of known risks and supporting data instead of letter categories. This update was designed to improve clinical decision-making and patient counseling (9).

Evidence from clinical studies is generally reassuring but still requires caution.

A retrospective cohort study including 826 pregnant women with glaucoma found no significant association between IOP lowering medication use and adverse neonatal outcomes such as congenital anomalies, preterm birth, or low birth weight. Similar findings were observed when prostaglandin analogues and β -blockers were analyzed separately. The results suggest no clear link between early pregnancy exposure to these medications and major neonatal harm (55).

A multicenter descriptive study of 114 pregnancies in 56 women with glaucoma or ocular hypertension reported that 82% of pregnancies involved exposure to at least one topical antiglaucoma medication. Commonly used agents included β -blockers, α -agonists, carbonic anhydrase inhibitors, and prostaglandin analogues. No significant associations were found between most treatments and adverse maternal or neonatal outcomes. However, α -agonist use was associated with higher rates of NICU admission, particularly when used in the third trimester (56).

A population-based case-control study evaluating low birth weight (LBW) included 244 pregnant women treated with topical glaucoma medications and 1,952 matched controls. After adjustment for confounders, β -blocker use was not associated with an increased risk of LBW (adjusted OR 1.48; 95% CI 0.86–2.56). In contrast, non- β -blocker therapies were associated with a higher risk of LBW (adjusted OR 2.15; 95% CI 1.05–5.00), supporting β -blockers as a preferred first-line option when treatment is required during pregnancy (57).

Safety concerns also extend beyond active ingredients to preservatives, particularly benzalkonium chloride (BAK). BAK concentrations in ophthalmic solutions range from 0.004% to 0.02% and are known to disrupt the tear film and contribute to ocular surface disease. Animal studies have shown dose-dependent fetotoxic effects at high exposures, including minor skeletal abnormalities, although no major malformations were observed (9,52). Therefore, minimizing topical exposure and systemic absorption during pregnancy is strongly recommended.

Simple measures can significantly reduce systemic absorption of eye drops. Techniques such as nasolacrimal occlusion, punctal occlusion, or eyelid closure for five minutes after instillation can reduce systemic uptake by more than 60% (9). These methods are safe, easy

to perform, and should be routinely recommended for pregnant patients using topical glaucoma therapy.

Table 2. FDA classification for medications in relation to teratogenic risk (9).

Category A	drugs are the safest. Studies in pregnant women show they do not harm the fetus.
Category B	drugs are also generally safe. Animal studies may show some risk, but studies in humans do not, or there is no evidence of harm so far.
Category C	drugs have uncertain safety. There isn't enough research in humans, and animal studies may show possible harm. The potential benefits may justify the potential risk.
Category D	drugs are known to have risk to the fetus, but in serious situations, a doctor may still prescribe them if the mother's health depends on it.
Category X	drugs are dangerous in pregnant and must not be used because they are proven to cause harm to the fetus.
FDA: US Food and Drug Administration.	

6.7.5.1 Prostaglandin Analogues and Prostaglandins

Prostaglandin analogues such as latanoprost, travoprost, bimatoprost, and tafluprost are widely used as first-line treatments for glaucoma in non-pregnant patients because of their strong and reliable ability to lower IOP. These medications are synthetic analogues of prostaglandin F_{2α} and work primarily by increasing uveoscleral outflow (9,33,34,40). Despite their proven effectiveness, their use during pregnancy remains controversial. These drugs can cross the placental barrier, raising concerns about potential effects on the fetus. By interacting with prostaglandin F_{2α} receptors, they may stimulate uterine smooth muscle contraction, exhibit luteolytic effects, and promote oxytocin release. Together, these mechanisms provide a biologically plausible explanation for possible risks such as premature labor or spontaneous abortion (9).

Newer prostaglandin-based agents, such as latanoprostene bunod, combine traditional prostaglandin activity with nitric oxide-mediated enhancement of trabecular outflow. While this dual mechanism provides slightly greater IOP reduction than latanoprost alone, its safety profile in pregnancy remains uncertain. Although nitric oxide plays a beneficial physiological role in uterine and placental blood flow, this formulation results in higher systemic exposure to latanoprost acid and therefore does not appear to offer a clear safety advantage during pregnancy (9,34).

For these reasons, prostaglandin analogues including newer derivatives continue to be classified as FDA Category C and are generally avoided during pregnancy unless the potential benefits clearly outweigh the risks Table 2 (9). During lactation, animal studies suggest that these drugs may be excreted in breast milk, but definitive human data are lacking. Most clinicians consider their use acceptable with caution, given their minimal systemic absorption when administered topically (9,34).

6.7.5.2 *Beta-Blockers*

Topical beta-blockers, such as timolol, levobunolol, carteolol, metipranolol, and betaxolol, remain important medications in the treatment of glaucoma. These drugs lower IOP by reducing aqueous humor production through inhibition of cyclic AMP in the ciliary epithelium. Most are non-selective beta-blockers, except for betaxolol, which is relatively selective for β_1 receptors (9,33,34,42).

Beta-blockers are also commonly used in obstetric practice, particularly for managing pregnancy-induced hypertension. This widespread systemic use offers some reassurance about their safety; however, potential risks to the fetus and newborn have been reported. These include growth restriction, low birth weight, lethargy, respiratory depression, and, in rare cases, bradycardia and cardiac rhythm disturbances, as illustrated in Table 4.

When a beta-blocker is required during pregnancy, timolol gel-forming formulations administered once daily are often preferred, as they provide effective IOP control with reduced systemic exposure. During breastfeeding, timolol and other beta-blockers can accumulate in breast milk. Although they are not absolutely contraindicated, infants should be closely monitored for signs of systemic beta-blockade, such as lethargy, feeding difficulties, or slow heart rate (9,34).

6.7.5.3 *Alpha-2 Adrenergic Agonists*

Brimonidine occupies a unique position among glaucoma medications used during pregnancy, as it is classified as FDA Category B Table 2. It works by reducing aqueous humor production and increasing uveoscleral outflow, making it an effective option for IOP (9,33,34,42).

Because brimonidine can cross the blood brain barrier, there are concerns regarding potential central nervous system effects in newborns. As a result, it is generally considered acceptable for use during early pregnancy but should be discontinued before delivery Table 3. Due to the

risk of secretion into breast milk and the potential for apnea or sedation in infants, brimonidine is usually avoided during breastfeeding (9).

6.7.5.4 *Carbonic Anhydrase Inhibitors*

CAIs are available in both topical forms (dorzolamide, brinzolamide) and systemic forms (acetazolamide, methazolamide). These medications lower intraocular pressure by reducing aqueous humor production through inhibition of carbonic anhydrase in the ciliary processes (9,33,34,42).

Systemic CAIs carry a higher risk during pregnancy, and their use is generally avoided unless necessary (9,42). Additional concerns include potential neonatal metabolic disturbances, such as renal tubular acidosis, when systemic exposure occurs Table 4 (9,42).

Topical CAIs have much lower systemic absorption and are therefore preferred when this drug class is required. However, they remain classified as FDA Category C Table 1. For this reason, many clinicians avoid their use during pregnancy Table 3 and reserve them for later stages only when necessary. When prescribed, techniques such as punctal occlusion are often recommended to further reduce systemic exposure (9,34,42).

During breastfeeding, acetazolamide is generally considered compatible with nursing according to pediatric guidelines, although monitoring the infant for possible side effects is advised Table 4 (9,34,42).

6.7.5.5 *Parasympathomimetics*

Cholinergic agents, once widely used in glaucoma treatment, are now rarely prescribed. These medications can interact with cholinergic receptors in the placenta, which play a role in prostaglandin release and regulation of placental blood flow. Because of their poor tolerability and potential teratogenic effects, cholinergic agents are generally avoided during pregnancy due to its neurological side effects in newborns have further limited their use in the postpartum period Table 4 (9,33,34,42).

6.7.5.6 *Rho-Kinase Inhibitors*

Rho-kinase inhibitors, such as netarsudil, are a newer class of glaucoma medications that work primarily by increasing trabecular outflow. The Rho-kinase pathway is also involved in uterine contractility, raising theoretical concerns regarding potential effects during

pregnancy. The overall safety profile for the fetus remains poorly defined due to limited available data (9,33,34,42).

Because of the lack of human pregnancy data and the potential risk of fetal harm, these medications are currently not recommended for use during pregnancy or while breastfeeding (9,42).

Table 3. Stage wise choice of anti-glaucoma medicines (9).

Medication class	First trimester	Second trimester	Third trimester	Lactation
Alpha-2 adrenergic agonist	First line	Avoid	Avoid	—
Beta-blockers	Second line	Second line	Second line, monitoring for fetal growth, and HR	First line (but avoid in heart disease)
Prostaglandin analogs	Avoid	Third line	Avoid during last phase	First line
Topical carbonic anhydrase inhibitors	Avoid	Third line	First line, monitoring for neonatal acidosis	First line
Systemic carbonic anhydrase inhibitors	Limited time, for acute need only	PRN uncontrolled on topical therapy	First line	—

Table 4. Potential Adverse Effects of IOP-Lowering Medications During Pregnancy and Breastfeeding (9).

Drug Class	Pregnancy – Animal Studies	Pregnancy – Theoretical Risk / Human	Breast feeding – Reported Effects	FDA Classification
Parasympathetic agents	Teratogenic	Dysregulation of placental perfusion	Seizures, fever, diaphoresis reported in newborns	Category C
Sympathetic agents – brimonidine	No significant effect	Delay in labor / uterine hypotony	CNS depression, hypotension, apnea in infants	Category B
Prostaglandin analogues	High incidence of miscarriage	Uterine contractions	No reported side effects	Category C
β blockers	Delayed fetal ossification, fetal resorption	Cardiac rhythm changes, respiratory effects	Arrhythmia, bradycardia, impaired respiratory control in newborns; controversy over breast milk concentrations	Category C
Carbonic anhydrase inhibitors – topical	Decreased fetal weight; vertebral body malformations	Lower fetal weight	No reported side effects	Category C
Carbonic anhydrase inhibitors – oral	Forelimb anomalies, limb malformations	One case of teratoma reported	No reported side effects	Category C

6.7.6 Advantages and Disadvantages of Drug Therapy for Glaucoma

Drug therapy remains the mainstay of glaucoma management, with prostaglandin analogues providing the strongest IOP lowering effect among topical agents. The 2025 European Glaucoma Society (EGS) guidelines recommend consistent use of either monotherapy or combination therapy, although they do not distinguish between preserved and preservative-free formulations and predate newer non-pharmacological approaches such as MIGS (26).

Long term adherence is essential for treatment success, but glaucoma is often asymptomatic in its early stages, meaning visual field loss may go unnoticed by patients. Adherence rates are generally low: up to 50% of newly diagnosed patients do not attend follow-up visits, and many prescriptions for IOP lowering drops are never filled. Even with prostaglandin analogues the most effective topical class only about 30% of patients remain adherent after 24 months. Poor adherence is associated with older age, cognitive or motor impairment, multiple comorbidities, longer disease duration, and dependence on caregivers (26).

Treatment complexity also plays a major role. Patients on multiple medications or frequent dosing schedules often struggle with correct administration, while combination therapies may help reduce this burden. Local side effects such as conjunctival hyperemia, ocular surface irritation, and discomfort further reduce compliance. Preservatives, particularly benzalkonium chloride (BAK), can destabilize the tear film, contribute to dry eye disease, affect deeper corneal layers, and occasionally trigger allergic reactions. Preservative-free formulations are generally better tolerated, although single-dose units may be less convenient to use (26).

Despite these limitations, topical drug therapy remains highly effective when adherence is good. Patients should be properly educated about the importance of consistent use, possible side effects, and available alternatives or adjunctive options, including non-pharmacological treatments such as MIGS, to improve long term outcomes (26).

The management of glaucoma during pregnancy adds further complexity, requiring careful balancing of maternal visual preservation with fetal safety.

A questionnaire-based study among UK consultant ophthalmologists illustrated real world practice patterns. Of 282 respondents, just over a quarter reported experience managing pregnant glaucoma patients, indicating that although uncommon, it is a relevant clinical scenario. Most clinicians opted to continue existing therapy, while a significant proportion preferred observation alone, reflecting individualized decision-making based on disease severity and perceived risk.

Considerable uncertainty was also noted. Nearly one third of respondents were unsure how they would manage such cases, highlighting the lack of clear consensus. Among those initiating treatment, β -blockers were most chosen as first-line therapy, followed by prostaglandin analogues. These findings emphasize variability in clinical practice and the need for clearer guidance, while reinforcing that management must remain individualized (54).

6.7.7 Laser treatment of glaucoma in pregnancy

Laser treatment options for glaucoma include Nd:YAG laser iridotomy, diode laser cyclophotocoagulation, and laser trabeculoplasty, which encompasses ALT, SLT, and micro pulse diode trabeculoplasty. Nd:YAG laser iridotomy is mainly indicated in narrow-angle or angle-closure glaucoma, as it creates an alternative pathway between the posterior and anterior chambers to improve aqueous outflow. Diode laser cyclophotocoagulation reduces aqueous production by partially ablating the ciliary body processes and may be considered in refractory cases or as an alternative to surgery (11).

Among trabeculoplasty techniques, ALT delivers focal thermal burns to the trabecular meshwork, inducing structural changes and coagulation. SLT selectively targets pigmented trabecular cells with minimal thermal damage to surrounding tissue and has largely replaced ALT due to similar efficacy and a better safety profile. Micro pulse diode trabeculoplasty further reduces thermal diffusion and limits tissue damage.

Reports of laser use in pregnancy suggest that these procedures can be effective and safe in selected cases. Nd:YAG laser iridotomy has been successfully performed in angle-closure glaucoma, while diode laser cyclophotocoagulation has been used in refractory disease (11,58). In addition, studies involving pregnant, breastfeeding, or pregnancy-planning women with POAG or OHT have shown that SLT and ALT can significantly reduce IOP and decrease the need for topical medications (11,59,60). In some cases, adequate IOP control was maintained without pharmacological therapy throughout pregnancy and into the postpartum period.

Despite these advantages, laser trabeculoplasty has limitations in women of reproductive age. Its effectiveness is generally lower in patients under 40 years and depends on an open, structurally intact anterior chamber angle, which may not be present in many younger patients with congenital or secondary glaucoma. The delayed onset of effect also limits its usefulness when rapid IOP reduction is required. In addition, the need for topical anesthetics

and perioperative medications may introduce potential risks during pregnancy. Finally, its effect may be temporary and may not extend beyond the pregnancy period in all cases (11,33).

6.7.8 Surgical Management for Glaucoma in Pregnancy

The main objectives in glaucoma management are preservation of visual function and quality of life, while ensuring safety for both mother and fetus. During pregnancy and breastfeeding, these objectives require careful individualization and close monitoring to balance maternal and fetal considerations (26).

Surgical treatment is reserved for cases in which IOP remains uncontrolled despite maximal medical and laser therapy, particularly when there is evidence of progressive visual field loss or risk to central vision (11).

Among surgical options, trabeculectomy involves creating a controlled fistula to allow aqueous humor to drain from the anterior chamber into a subconjunctival bleb, thereby reducing IOP. Tube shunt surgery uses an implanted drainage device that directs aqueous humor from the anterior chamber to an external reservoir plate under the conjunctiva, enabling long-term controlled outflow and pressure reduction.

MIGS is often preferred when appropriate due to its more favorable safety profile and limited tissue disruption. Although the IOP reduction is generally more modest compared to traditional surgery, MIGS is associated with fewer complications and faster recovery, making it particularly suitable in pregnancy (11,25,26).

The choice of surgical approach should be guided by disease severity, risk of progression, and safety considerations for both mother and fetus (11).

6.7.8.1 *Use of Anesthesia*

Pregnancy induces physiological changes that increase maternal susceptibility to hypoxia, hypercapnia, and systemic hypotension, placing both mother and fetus at higher risk during anesthesia, particularly general anesthesia. Additional challenges include difficult airway management due to gastroesophageal reflux and a heightened risk of aspiration. Many anesthetic agents, including narcotics, neuromuscular blockers, and inhalational anesthetics, can cross the placenta, potentially causing fetal cardiovascular or central nervous system depression.

Although well controlled human studies on teratogenicity are lacking, some reports suggest a higher incidence of low birth weight and neural tube defects following first-trimester exposure to general anesthesia (51). In contrast, local anesthetics commonly used in ophthalmic procedures are generally considered safe, with no evidence of teratogenicity. However, bupivacaine has been associated with transient fetal bradycardia, whereas lidocaine has not. Topical anesthesia, supplemented by subconjunctival or anterior sub-Tenon's blocks, minimizes systemic absorption. Therefore, it is recommended to use the lowest effective dose of local anesthetic to ensure analgesia while limiting fetal exposure. (30,33)

6.7.8.2 *Microinvasive Glaucoma Surgery During Pregnancy*

MIGS includes a range of procedures targeting different parts of the aqueous outflow system. Trabecular-based techniques, such as Trabectome, GATT, and the OMNI system, aim to bypass or remove diseased trabecular meshwork to restore physiological outflow.

MIGS can be broadly classified into three anatomical categories (26):

Trabecular (Schlemm's canal) devices enhance physiological outflow with a low risk of hypotony and are typically used in mild to moderate glaucoma, particularly in patients with low baseline IOP, medication intolerance, or poor adherence. Suprachoroidal devices increase uveoscleral outflow and offer greater IOP reduction but carry a higher risk of transient hypotony or hyphemia; they are generally reserved for patients with mild to moderate glaucoma and higher baseline IOP. Subconjunctival devices create an alternative drainage pathway to a bleb, often using mitomycin C to reduce fibrosis, and are more suitable for advanced glaucoma or cases requiring lower target IOP when other MIGS options are insufficient.

Common MIGS devices include iStent, Hydrus, iStent Supra, XEN, and PreserFlo, which differ in drainage pathway, material, and indication. Although long-term data are still limited, particularly for suprachoroidal devices, MIGS can reduce dependence on topical medications, improving adherence and quality of life (26). Schlemm's canal devices such as iStent and Hydrus Microstent create microchannels that enhance aqueous outflow with minimal disruption to ocular structures (15,16).

These procedures typically achieve moderate but clinically meaningful IOP reduction and often decrease the need for topical therapy, which is particularly advantageous during pregnancy, where minimizing systemic drug exposure is important (15,16).

More advanced MIGS options, often referred to as minimally invasive bleb surgery (MIBS), such as the XEN Gel Stent and PreserFlo MicroShunt, create subconjunctival or suprachoroidal drainage pathways. While they may achieve greater IOP reduction, their long-term success often depends on antimetabolites, which are generally avoided during pregnancy. For this reason, they are reserved for progressive disease when other options are insufficient (15,16,26).

MIGS offers a favorable balance of safety, tissue preservation, and limited anesthetic requirements, making it a practical surgical option in selected pregnant patients. Although it may not always achieve the very low target pressures seen with traditional filtering surgery, it provides meaningful IOP reduction with lower perioperative risk and reduced fetal exposure (15,16).

MIGS procedures are characterized by minimally invasive corneal entry, limited tissue trauma, biocompatible implants that support natural outflow, moderate IOP reduction, favorable safety profiles, and rapid recovery. As with all glaucoma interventions, target IOP should be individualized based on disease stage, progression, age, and risk profile. Early disease typically requires at least a 20% reduction in IOP, moderate disease around 30%, and advanced disease even greater reduction (26).

Success depends on surgical expertise and careful postoperative management. Experience is particularly important for subconjunctival techniques, which require precise placement and close follow-up.

MIGS should be viewed as a complementary option to traditional surgery, particularly in early or moderate glaucoma or when medication control is insufficient. Conventional filtering surgery remains the standard for advanced disease or when substantial IOP reduction is required (26).

6.7.8.3 Trabeculectomy Surgery

Trabeculectomy is a filtration surgery used in glaucoma management to achieve long-term reduction of IOP when medical or laser treatment is insufficient. It is usually performed as a day-case procedure in an operating theatre. The aim is to slow or halt progression of glaucomatous optic neuropathy by improving aqueous outflow, rather than restoring lost vision.

The procedure involves creating a partial-thickness scleral flap and a controlled fistula between the anterior chamber and the subconjunctival space. The scleral flap is then secured

with sutures to regulate outflow, and the conjunctiva is closed to form a functional filtration system. Postoperatively, aqueous humor drains into the subconjunctival space, where it collects as a filtering bleb and is gradually absorbed into the episcleral circulation, resulting in a sustained reduction in IOP (11,44).

During pregnancy, trabeculectomy is generally reserved for cases of uncontrolled or rapidly progressive glaucoma despite maximal tolerated medical therapy and/or laser treatment. Its use is limited by concerns related to anesthesia exposure, fetal safety considerations, and altered wound healing during pregnancy. In selected severe or refractory cases, trabeculectomy without antimetabolites has been performed, although this approach is used cautiously (11).

Pregnancy may also increase the risk of surgical failure, likely due to hormonal influences on conjunctival wound healing that promote fibrosis and may compromise bleb function. For this reason, the decision to proceed with surgery requires careful individual risk–benefit assessment, considering both disease severity and gestational age (11).

6.7.8.4 Role of Glaucoma Drainage Devices

Recent surgical literature suggests that glaucoma drainage devices offer more predictable postoperative outcomes in patients who are at high risk for scarring, including younger individuals and pregnant patients (26,27). Because these devices do not depend on antimetabolites for success, they may be more suitable than trabeculectomy in certain clinical situations. Nevertheless, implantation still requires conjunctival manipulation and carries inherent surgical risks and is therefore generally reserved for refractory or advanced cases.

Evidence from glaucoma surgery in complex eyes such as those with prior corneal transplants further highlights the importance of individualizing surgical strategies based on factors such as wound healing potential, the need to achieve low target intraocular pressures, and long-term structural stability. These same principles are directly applicable to surgical decision-making in pregnant patients (27,28).

6.7.8.5 Challenges of Glaucoma Surgery During Pregnancy and Lactation

Glaucoma surgery during pregnancy presents multiple challenges that can increase surgical complexity and raise the risk of failure, while also complicating perioperative management. Younger maternal age is associated with more rapid wound healing, which can increase the likelihood of bleb fibrosis and subsequent surgical failure.

Women of reproductive age are more commonly present with congenital, juvenile, syndromic, or secondary forms of glaucoma, which are generally associated with less favorable surgical outcomes.

Pregnancy related physiological changes may further influence healing responses. Increased levels of vascular endothelial growth factor and placental growth factor may enhance tissue repair but also promote fibrosis at surgical and bleb sites, increasing the risk of postoperative failure. Tissue edema during the second and third trimesters can also make surgical manipulation more difficult.

Maternal positioning during surgery introduces additional concerns. Supine positioning may compress the aorta and inferior vena cava, potentially leading to hypotension and reduced uteroplacental perfusion, increasing the risk of fetal compromise. Pregnant patients also have an increased risk of thromboembolic events, often requiring prophylactic measures such as compression stockings or pneumatic devices. In addition, gastroesophageal reflux and increased aspiration risk, particularly in late pregnancy, complicate anesthetic management. Both local and general anesthesia carry potential risks for mother and fetus, requiring careful perioperative planning and close interdisciplinary collaboration. Pre- and postoperative medications must also be selected with caution to minimize fetal exposure and reduce the risk of neonatal complications (11).

6.7.8.6 Considerations in Glaucoma Surgery During Pregnancy

6.7.8.6.1 Preoperative Preparation

The initial step in planning glaucoma surgery during pregnancy is selecting an intervention that is both effective in controlling IOP and safe for the mother and fetus. Although trabeculectomy remains the conventional surgical standard for glaucoma management, its success in younger patients may be reduced due to a stronger wound healing response and the limited use of antifibrotic agents during pregnancy. As a result, valved glaucoma drainage devices may be considered in cases of refractory glaucoma when traditional filtration surgery is less likely to succeed (11,30). Trabeculectomy performed without antimetabolites may still achieve adequate short-term IOP control, although the risk of long-term scarring and surgical failure remains higher. Other consideration in surgical planning is whether to operate on one eye or both eyes. Performing surgery on both eyes during the same session could theoretically reduce anesthesia exposure and the number of postoperative visits, which may become more difficult as pregnancy advances. However, simultaneous bilateral intraocular

surgery is generally avoided due to ethical concerns and the risk of bilateral complications. Therefore, the outcome of the first procedure often guides the timing and necessity of surgery in the second eye (11,30).

Preoperative planning should include close collaboration between the ophthalmologist, obstetrician, and anesthesiologist to ensure optimal maternal and fetal safety. Maintaining adequate hydration and establishing reliable intravenous access are also important aspects of perioperative care (11,30).

6.7.8.6.2 Intraoperative Considerations

Maternal positioning during surgery requires particular attention. In the second and third trimesters, the enlarged uterus may compress the aorta and inferior vena cava when the patient is lying flat, potentially resulting in systemic hypotension and reduced uteroplacental blood flow. To minimize this risk, the patient's body can be slightly rotated toward the left lateral position, while maintaining a stable head position for ophthalmic surgery.

Pregnant patients also have an increased tendency toward gastroesophageal reflux, which raises the risk of aspiration during surgical procedures. Therefore, appropriate precautions should be taken to avoid surgery when the stomach is full. Although intraoperative fetal heart monitoring may be considered in certain cases, it is not always necessary because most ophthalmic procedures are relatively short.

When possible, glaucoma surgery is usually postponed until the second trimester, as this period is associated with a lower risk of teratogenic effects from anesthetic exposure compared with early pregnancy. Nevertheless, surgical complexity may increase later in pregnancy due to physiological and anatomical changes (11,30).

6.7.8.6.3 6.7.8.6.3 Use of Antimetabolites

Antifibrotic agents such as mitomycin C and 5-fluorouracil are commonly used during trabeculectomy to reduce postoperative scarring and improve surgical outcomes. However, their use during pregnancy is generally discouraged due to the potential risk of fetal toxicity. Although direct evidence of teratogenic effects following subconjunctival application is limited, the pharmacological properties of these agents suggest possible risks to fetal development.

Because younger patients often exhibit a stronger wound healing response, avoiding antifibrotic agents may increase the likelihood of postoperative fibrosis and filtration failure. In this context, alternative approaches to wound modulation may be considered. One

potential option is the biodegradable collagen matrix implant (Ologen), which functions as a scaffold that regulates fibroblast activity and helps prevent excessive subconjunctival fibrosis. Although studies in nonpregnant populations have demonstrated outcomes comparable to those achieved with mitomycin C, there is currently no clinical evidence regarding the safety or effectiveness of Ologen implants in pregnant patients (11,30). Pregnancy related tissue edema may also complicate surgical procedures by making scleral and conjunctival suturing more difficult. These changes can influence postoperative healing and bleb formation. The use of releasable sutures may therefore be beneficial, allowing better control of aqueous filtration and intraocular pressure during the postoperative period (11, 30).

6.7.8.6.4 Postoperative Medications

Postoperative medications should be carefully selected to minimize fetal exposure, and these may include the following agents:(11,30)

Antibiotics:

Topical antibiotics are commonly prescribed after glaucoma surgery to prevent infection. Erythromycin is generally considered a safer option in pregnancy because it crosses the placental barrier poorly and has not been associated with congenital abnormalities. Although topical fluoroquinolones have not shown clear evidence of teratogenic effects, data regarding their safety in pregnancy remain limited. Antibiotics such as tetracyclines and aminoglycosides should be avoided due to known fetal risks (11,30).

Corticosteroids:

Topical corticosteroids are routinely used following glaucoma surgery to control inflammation and promote appropriate wound healing. Current evidence suggests that topical steroid therapy can be used during pregnancy, as systemic absorption is minimal. If systemic corticosteroid therapy becomes necessary, prednisolone or methylprednisolone are generally preferred because they cross the placenta less readily than dexamethasone or betamethasone. Nevertheless, systemic steroids should be administered with caution (11,30).

Cycloplegic agents:

Cycloplegic medications may be used to stabilize the anterior chamber and reduce postoperative inflammation. Homatropine is often favored over atropine because atropine has been associated with fetal bradycardia in certain situations (130).

6.7.9 Postpartum and Lactation Considerations

6.7.9.1 *General Postpartum Glaucoma Considerations*

The postpartum period is important for women with glaucoma because rapid hormonal changes can significantly affect IOP. A rebound increase in IOP may occur after delivery, particularly in women with pre-existing disease or advanced optic nerve damage, making early and frequent monitoring essential to prevent further damage (20,42).

Changes in corneal thickness and curvature can also occur postpartum, and careful clinical assessment is required to distinguish physiologic changes from true glaucomatous progression (20).

6.7.9.2 *Postpartum Monitoring Overview*

The European Glaucoma Society guideline supports structured follow-up after delivery to ensure long-term stability of glaucoma (42):

1–2 weeks postpartum: IOP measurement and optic nerve evaluation to detect early rebound pressure rises

4–6 weeks postpartum: Visual field testing and therapy reassessment to detect functional progression

3 months postpartum: Comprehensive ophthalmic examination to confirm IOP stability and optic nerve health).

6–12 months postpartum: Repeat OCT and visual field testing to detect delayed structural or functional changes

Hormonal changes during pregnancy can temporarily reduce IOP through increased uveoscleral outflow. After delivery, the abrupt drop in estrogen and progesterone may lead to rebound increases in IOP, placing the optic nerve at risk if not closely monitored. Clinicians must carefully interpret postpartum structural and functional changes to distinguish normal physiologic recovery from true disease progression (20).

6.7.9.3 *Safety of Anti-Glaucoma Medications during Lactation*

Anti-glaucoma treatment during breastfeeding requires careful consideration because small amounts of medication can pass into breast milk. The European Glaucoma Society notes that although reported exposure is usually low (often <1–2% of the maternal dose), newborns may still be more vulnerable due to immature liver and kidney function and an

underdeveloped blood brain barrier (42,11). This makes clinical decision-making more cautious in the early postpartum period.

A key issue is that topical eye drops are not fully local treatments. A significant proportion (around 35–80%) can be systemically absorbed through the nasolacrimal system, bypassing first pass metabolism. For this reason, simple measures such as punctal occlusion or keeping the eyelids closed for a minute or two after instillation are recommended to reduce systemic absorption. Once-daily dosing, when appropriate, may also help limit exposure (42,11).

Timolol is the most widely used topical β -blocker and is known to pass into breast milk. Although the infant dose is usually low, cases of bradycardia, apnea, and hypotension have been reported, particularly in premature or medically fragile infants. For this reason, it is generally used with caution, but it is not absolutely contraindicated during breastfeeding when monitoring is in place Table 5 (42,11).

Brimonidine is more problematic. It is excreted into breast milk and has been linked to central nervous system depression in infants, including drowsiness, apnea, and hypotension. Because newborns have limited ability to metabolize the drug, it is usually avoided during breastfeeding, especially in infants under two months (42,11).

Prostaglandin analogues such as latanoprost appear safer in comparison. Evidence of harm in humans is lacking, and systemic exposure is expected to be low due to rapid breakdown of the drug. They are generally considered acceptable when clinically needed (42,11).

Carbonic anhydrase inhibitors depend on formulation. Oral acetazolamide does enter breast milk but in small amounts and is usually considered compatible with breastfeeding, though caution is advised in vulnerable infants. Topical agents like dorzolamide result in even lower exposure but are still used cautiously, particularly in preterm infants (42,11).

Risks depend not only on the drug itself but also on infant maturity, dosing frequency, and maternal metabolism. Drugs affecting the cardiovascular or nervous system especially β -blockers and α_2 -agonists require the most caution. In contrast, prostaglandin analogues and topical carbonic anhydrase inhibitors are generally preferred when treatment is needed during lactation.

Timolol may be used with monitoring, brimonidine is usually avoided, latanoprost can be used when necessary, and acetazolamide is reserved for cases where other options are insufficient (42,11).

Table 5. General lactation safety guidance (42).

Medication Class	Lactation Safety	Clinical Considerations
Beta-blockers (timolol)	Compatible with caution	Use lowest effective dose; apply punctal occlusion; monitor infant
Alpha-2 agonists (brimonidine)	Not recommended	Potential CNS depression in infants; avoid
Prostaglandin analogues (latanoprost, travoprost)	Limited data	Use cautiously; consider non-pharmacological alternatives
Topical carbonic anhydrase inhibitors (dorzolamide)	Limited data	Prefer topical; monitor for systemic exposure
Systemic carbonic anhydrase inhibitors (acetazolamide)	Avoid	High systemic absorption; potential infant risk

6.7.9.4 Recommendations for Postpartum and Lactating Women with Glaucoma

Postpartum management of glaucoma should focus on early identification of disease progression, with regular follow-up examinations and attention to IOP fluctuations and visual field changes. Treatment decisions during this period should be cautious, with preference given to medications considered compatible with breastfeeding. Techniques such as nasolacrimal occlusion can be used to limit systemic absorption and reduce infant exposure (12,42).

Whenever clinically appropriate, the treatment burden should be reduced, either by lowering the number of medications or temporarily discontinuing therapy under close supervision of IOP and disease status. Patients may be advised to administer eye drops immediately after breastfeeding to further minimize exposure. SLT can also be considered as a means of reducing or eliminating the need for ongoing topical therapy.

Topical β -blockers and carbonic anhydrase inhibitors are commonly used first-line options, although β -blockers should be used with caution in infants at risk of cardiovascular or respiratory complications. Oral carbonic anhydrase inhibitors may be considered in selected cases when additional IOP control is required. Prostaglandin analogues are generally reserved for situations where further reduction in IOP is needed as part of combination therapy. Brimonidine should be avoided during lactation due to the risk of central nervous system depression in infants (11).

Regular follow-up during the first year postpartum is important to ensure disease stability and to adjust treatment if progression occurs (12,42). In cases where long-term medication use is undesirable or disease control is insufficient, laser procedures or MIGS may provide alternative options (15,16,42).

Lifestyle measures can also support overall disease management. Adequate sleep, balanced nutrition, blood pressure control, and smoking cessation should be encouraged, as these factors contribute to both ocular and systemic health (7,42).

Management should ideally involve a multidisciplinary approach to ensure effective disease control while maintaining safety for both mother and infant (12,42).

7 Prognosis and Follow-Up of Glaucoma in Pregnancy

The course of glaucoma during pregnancy is not uniform and is influenced by both physiological changes and modifications in treatment. Hormonal and systemic vascular adaptations may lead to a modest reduction in IOP, mainly through increased uveoscleral outflow and reduced episcleral venous pressure. However, this effect is unpredictable, and apparent IOP improvement does not necessarily indicate disease stability (11,12,42).

Evidence suggests that disease progression is more likely to occur after delivery, particularly in women who discontinue topical therapy during pregnancy. In a retrospective study of 37 women with open-angle glaucoma, progression of structural or functional damage was observed in 28.4% of eyes at a mean of 14 months postpartum, whereas no progression was detected during pregnancy. Higher IOP levels, especially in the second and third trimesters, as well as greater IOP variability, were associated with later deterioration (39).

In contrast, patients who continued treatment or only partially reduced medication tended to remain stable. In a smaller cohort of eight patients (13 eyes), 87.5% showed no progression. Mean IOP remained relatively consistent throughout pregnancy (17.3 ± 3.6 mmHg pre-pregnancy and 17.4–20.2 mmHg during gestation, with no significant difference). Although the number of medications was reduced from 1.7 to 0.83 agents on average ($p = 0.04$), disease control was generally maintained (53).

There are isolated reports describing possible fetal effects associated with topical glaucoma therapy. One case of intrauterine growth restriction occurred in a patient treated throughout pregnancy with a fixed combination of timolol and dorzolamide, although a direct causal

relationship could not be established. Nevertheless, this case highlights that even topical agents may have systemic effects and potential fetal implications (53).

The disease course appears to be most strongly influenced by IOP stability, magnitude of fluctuation, and changes in treatment exposure during pregnancy. For this reason, close monitoring is essential throughout gestation and particularly after delivery. Regular assessment of IOP, optic nerve status, and visual fields is recommended, especially in women who reduce or discontinue therapy during pregnancy, as these patients may be at increased risk of delayed progression postpartum (39,42).

8 DISCUSSION OF RESULTS AND FUTURE RESEARCH

Pregnancy can influence IOP, optic nerve status, and glaucoma progression in complex and often unpredictable ways. Many women experience a physiological reduction in IOP during pregnancy, mainly related to hormonal changes (particularly estrogen and progesterone), increased plasma volume, and reduced episcleral venous pressure (11,12,42). These changes tend to enhance aqueous outflow, which may temporarily lower IOP.

However, this physiological effect is not consistent across patients and should not be considered protective. Some women with pre-existing glaucoma remain stable, while others show progression despite apparently favorable changes in IOP. This variability reflects the heterogeneous nature of glaucoma and reinforces the importance of individualized management rather than relying on expected physiological trends alone (32,42).

Monitoring remains central to care during pregnancy. OCT and fundus photography are valuable non-invasive tools for structural assessment, although interpretation should be cautious. Pregnancy-related physiological changes may subtly affect retinal nerve fiber layer measurements and optic nerve head appearance. Visual field testing remains essential for functional evaluation, but results can be more variable due to fatigue, discomfort, or reduced patient concentration (11,12,42).

Management is further complicated by the limited safety profile of available pharmacological treatments. No antiglaucoma medication can be considered completely risk-free during pregnancy. Among topical agents, β -blockers and α_2 -agonists are generally regarded as relatively safer, but both require caution due to systemic absorption and potential fetal or

neonatal cardiovascular and neurological effects. Prostaglandin analogues and systemic carbonic anhydrase inhibitors carry greater theoretical or documented risks, including effects on uterine activity, metabolic balance, and fetal development (11,12,22,42). As a result, treatment often follows a conservative stepwise approach, using the lowest effective dose and considering non-pharmacological options whenever possible.

Laser therapy plays an important role in this context. SLT and LPI are considered safe during pregnancy and can provide clinically meaningful IOP reduction without systemic drug exposure. SLT may reduce or eliminate the need for topical therapy. Nevertheless, transient IOP spikes and mild inflammation can occur, so appropriate follow-up of the patient is still required (11,12,22,42).

Surgical intervention is generally reserved for cases where disease continues to progress despite medical and laser therapy. MIGS has become an increasingly relevant option due to its favorable safety profile, limited tissue disruption, and reduced reliance on postoperative medications. It offers moderate IOP reduction and may be particularly suitable during pregnancy, especially in the second trimester when both maternal and fetal risks are relatively lower (25,26,30,42). In advanced or refractory disease, however, conventional filtering surgery may still be necessary despite its higher risk profile.

The postpartum and lactation periods also require careful attention. After delivery, hormonal changes may lead to rebound increases in IOP, particularly in patients with advanced or previously unstable disease. This makes structured follow-up essential, as delayed recognition of disease progression may result in irreversible optic nerve damage. Medication choices during breastfeeding add another layer of complexity, requiring ongoing balance between effective maternal treatment and minimization of neonatal exposure (11,12,18,42).

Despite growing clinical experience, evidence in this field remains limited. Most recommendations are based on retrospective studies, case series, and expert opinion rather than prospective controlled trials. Important gaps remain, particularly regarding the long-term safety of newer therapies, the optimal timing of surgical intervention such as MIGS, and the impact of pregnancy-related hormonal changes on optic nerve susceptibility and disease progression (11,12,32,42).

As a general results preserving vision in pregnant patients with glaucoma depends on early risk identification, careful monitoring, and individualized treatment planning that accounts for both maternal and fetal safety. Good outcomes rely on adherence to therapy, avoidance of unnecessary drug exposure, and timely escalation of treatment when progression is detected. Future research should priorities multicenter prospective registries, pharmacokinetic studies

during pregnancy and lactation, and the development of standardized, evidence-based guidelines. Strengthening collaboration between ophthalmology, obstetrics, pharmacology, and related specialties will be essential to improving care in this complex patient population (11,12,30,42).

9 CONCLUSION

Managing glaucoma during pregnancy poses a complex clinical challenge and requires a tailored, multidisciplinary strategy that effectively controls the disease while ensuring the safety of both the mother and the fetus.

In pregnancy hormonal fluctuations influence the dynamics of aqueous humor and ocular blood flow, which contribute to temporary decrease in intraocular pressure. However, this effect is not universal and does not exclude the risk of glaucoma progression, especially in women with underlying glaucoma.

Preconception evaluation of the baseline of IOP, the optic nerve condition, and the visual function are essential.

Management of glaucoma during pregnancy requires a cautious and stepwise approach.

Topical beta-blockers and alpha-2 adrenergic agonists are used as first-choice therapies in the first and second trimesters, however at least one-month prior labor, the latter must be replaced with local topical carbonic anhydrase inhibitors.

Laser interventions, including selective laser trabeculoplasty and laser peripheral iridotomy, are safe and can reduce dependence on anti-glaucoma medications during pregnancy and breast-feeding period.

In cases of severe or progressive disease, trabeculectomy may be performed preferably in the second trimester, although surgical intervention during pregnancy presents possible risks of anesthesia, postoperative medications and surgery failure. Trabeculectomy is still the gold standard in surgical glaucoma treatment, however minimally invasive glaucoma surgeries provide moderate reductions in intraocular pressure while allowing for potentially lower risk of complications and faster postoperative recovery.

Postpartum monitoring is crucial due to the rapid hormonal shifts that may cause variations in intraocular pressure. It is important to carefully adjust glaucoma medications while breastfeeding to safeguard maternal vision and reduce any potential risks to the infant.

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