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Ocular Changes in Pregnancy

Robert B. Dinn, BS,* Alon Harris, MSc, PhD† and Peter S. Marcus, MD‡

*Fourth Year Medical Student, Indiana University School of Medicine; †Professor, Glaucoma Research and Diagnostic Center, Departments of Ophthalmology and Physiology, Indiana University School of Medicine; and ‡Assistant Clinical Professor, Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, Indiana

Visual changes in pregnancy are common, and many are specifically associated with the pregnancy itself. Serous retinal detachments and blindness occur more frequently during preeclampsia and often subside postpartum. Pregnant women are at increased risk for the progression of preexisting proliferative diabetic retinopathy, and diabetic women should see an ophthalmologist before pregnancy or early in the first trimester. The results of refractive eye surgery before, during, or immediately after pregnancy are unpredictable, and refractive surgery should be postponed until there is a stable postpartum refraction. A decreased tolerance to contact lenses also is common during pregnancy; therefore, it is advisable to fit contact lenses postpartum. Furthermore, pregnancy is associated with a decreased intraocular pressure in healthy eyes, and the effects of glaucoma medications on the fetus and breast-fed infant are largely unknown.

Target Audience: Obstetricians & Gynecologists, Family Physicians

Learning Objectives: After completion of this article, the reader will be able to list the various ocular changes that occur during pregnancy, summarize the ocular disturbances that occur with preeclampsia and diabetes, and describe the management of some ocular problems during pregnancy.

INTRODUCTION

Visual disturbances are common among pregnant women (1, 2), and the physician should have a firm understanding of the various conditions associated with these disturbances. The ocular changes associated with pregnancy may offer insight into the pathophysiology of many diseases. Physicians should be able to distinguish among the different causes and delineate those conditions specifically associated with pregnancy. Several systemic disorders warrant ophthalmic referral in pregnant women; however, many visual disturbances in pregnant women require no treatment. Physicians should also understand that pregnancy influences the results of refractive eye surgery and that medications used to treat eye diseases may have effects on fetuses and breast-fed infants. This article discusses concerns specific to pregnancy and the eye, including preeclampsia, diabetic retinopathy, refractive eye surgery, contact lens intolerance, and glaucoma.

Reprint requests to: Peter S. Marcus, MD, Department of Obstetrics and Gynecology, Indiana University School of Medicine, 550 N. University Blvd, UH 2440, Indianapolis, IN 46202. Email: pmarcus@iupui.edu

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METHOD OF LITERATURE SEARCH

A MEDLINE search covering the years 1966 through 2002 was performed using the words pregnancy, preeclampsia, eye, eclampsia, diabetes, refractive eye surgery, PRK, LASIK, contact lens, and glaucoma. Additional references were obtained from the bibliographies of articles obtained in the MEDLINE search. Randomized controlled trials were given preference; however, nonrandomized noncontrolled trials and case studies were cited when no randomized controlled trials were available.

PREECLAMPSIA

Preeclamptic women may present with ocular disturbances including blurry vision, photopsia, diffuse retinal edema, decreased retinal arterial to vein ratio, serous retinal detachment, scotoma, and blindness (3–5). There is a worsening of visual disturbances with increasing severity of preeclampsia. In a retrospective study of 71 records of Japanese patients with severe preeclampsia or eclampsia, retinal pigment epithelial lesions were found in 36 eyes and serous retinal detachments were found in 40 eyes (4).

The mechanisms behind these changes are still being investigated, but vascular changes seem to be paramount. Possible causes stem from systemic conditions (hypertension, diabetes), cerebral autoregulatory, and/or hormonal changes. Jaffe and Schatz (3) suggest that the retinal changes in preeclamptic patients may be, at least partly, due to underlying systemic vascular diseases because many patients with preeclampsia have diabetes or chronic hypertension (Table 1). In a prospective, controlled, masked study excluding patients with diabetes and preexisting hypertension, Jaffe and Schatz (3) did not find evidence of hemorrhages, cotton-wool spots, exudates, Elschnig spots (yellow/hyperpigmented patches of retinal pigment epithelium overlying infarcted choriocapillaris lobules in hypertensive retinopathy), or retinal detachments in 31 patients with preeclampsia. In this same study, Jaffe and Schatz (3) found a statistically significant correlation between the reduction in arteriole to vein ratio and the diagnosis of severe preeclampsia ($P = .004$). Consistent with these results, Belfort and Saade (6) reported a case of retinal vasospasm during a period of visual disturbance in a preeclamptic woman. After the resolution of symptoms, central retinal arterial blood velocity increased and resistance decreased (6). Belfort et al. (7) also reported that magnesium, which is used as an antiseizure medication in preeclampsia, dilates the vessels distal to the central retinal and posterior ciliary arteries.

On the other hand, a breakthrough in cerebral autoregulation might be responsible for retinal changes (8).

TABLE 1 **Possible explanations for ocular changes in preeclampsia/eclampsia***

1. Coexisting/preexisting systemic vascular disease
2. Changes in hormonal milieu
3. Endothelial damage
4. Breakthrough in autoregulation
5. Hypoperfusion ischemia and/or hyperperfusion/edema

* The precise mechanism probably involves a combination of these factors.

Using color flow Doppler ultrasonography in 118 normotensive pregnant subjects, 20 preeclamptic subjects without visual symptoms, and 11 preeclamptic subjects with photophobia and retinal edema, Ohno et al. (9) concluded that preeclamptic women, especially those with photophobia, have orbital vascular vasodilation and/or hyperperfusion. These changes may be the reason behind the increased retinal edema and retinal detachments in preeclamptic women. Interestingly, the detachments may occur in the absence of retinal pigment epithelial lesions (4). Saito and Tano (4) propose that there are variable retinal pigment epithelial changes based on varying degrees of choroidal hypoperfusion. Retinal detachments without retinal pigment epithelial lesions might occur with less severe ischemia leading to changes in retinal pigment epithelium permeability.

Blindness has been reported to occur in almost 15% of women with eclampsia (5) and may occur postpartum (5, 10–12). Either compromise in retinal or occipital lobe vasculature is probably responsible. Case reports of transient blindness have been attributed to acute ischemic optic neuropathy (13) and retinal vasospasm and edema (14); however, most cases of blindness associated with preeclampsia and eclampsia are attributed to changes in the occipital cortex (5). The precise mechanism underlying cortical blindness is unknown. Based on a prospective study of women with blindness and pregnancy-induced hypertension, Cunningham et al. (5) concluded that transient cortical blindness resulted from petechial hemorrhages and focal edema in the occipital cortex. Similar to changes in the retina, two possible etiologies for focal edema are either vasospasm and ischemia or increased capillary permeability and edema. Using single-photon emission computed tomography, cerebral computerized tomography, and transcranial Doppler ultrasonography in 63 women with eclampsia, Naidu et al. (15) concluded that vasospasm with resultant ischemia led to cerebral edema in the watershed areas and parieto-occipital lobes causing seizures.

Interestingly, Borromeo et al. (10) described a case of cortical blindness in a preeclamptic patient complicated by hypotension and pointed out that the pathophysiology behind preeclampsia/eclampsia-induced blindness is different from watershed infarct-induced blindness. Apollon et al. (11) used neuroimaging to demonstrate that a case of cortical blindness in postpartum preeclampsia was the result of vasogenic cerebral edema. The authors (11) refuted the conclusion of Naidu et al. (15) because there was a question as to whether the imaging was done during the acute phase of changes. Kesler et al. (16) also

concluded that transient blindness in a preeclamptic pregnant patient was caused by vascular endothelial damage because severe proteinuria, recent placental thrombosis, and brain ischemia (based on computed tomography [CT] performed emergently and magnetic resonance imaging [MRI] performed several days after the return of vision) were present.

Using magnetic resonance imaging in 28 preeclamptic women with neurologic symptoms, Schwartz et al. (17) demonstrated that the presence of brain edema was associated with abnormal red blood cell morphology and elevated lactate dehydrogenase (LDH) levels. This suggested that microangiopathic hemolysis and endothelial damage were present, and endothelial damage may have resulted in a disturbed autoregulatory system (17). Interestingly, Edvinsson et al. (18) found that the posterior cerebral circulation contains fewer synapses with the sympathetic nervous system than does the anterior cerebral circulation, which could make this region more susceptible to the breakthrough of autoregulation (17). This finding is in agreement with the location of lesions detected in the parieto-occipital area by neuroimaging in patients with cortical blindness (5, 11, 12, 16, 17).

Posterior leukoencephalopathy syndrome, which consists of headache, altered mental functioning, seizures, and loss of vision (including cortical blindness), has been described in patients receiving immunosuppressive therapy or interferon and in patients with eclampsia or hypertensive encephalopathy associated with renal disease (19). This syndrome occurred postpartum in the eclamptic patients; however, the pathophysiology behind this syndrome probably is similar to the visual disturbances that occur before delivery. In fact, posterior leukoencephalopathy may be a variant of a broader syndrome of hypertensive/hyperperfusion encephalopathy (20).

Additionally, the hormonal changes of pregnancy influence ocular hemodynamics, which might provide insight into the pathophysiology of preeclampsia. By changing the production of endothelial-derived substances such as nitrous oxide, endothelin-1, and eicosanoid, estrogen has been demonstrated to lead to vasodilation (21–23). In a study using Doppler imaging analysis in 16 postmenopausal women on hormone replacement therapy, 16 postmenopausal women without hormone replacement therapy, and 20 young nonpregnant women, Harris-Yitzhak et al. (24) concluded that estrogen therapy in postmenopausal women apparently reduces vascular resistance distal to the ophthalmic artery to levels matching those of young women. Furthermore, Centofanti et al. (25) demonstrated that pulsatile ocular blood flow increased throughout pregnancy using information from 27 healthy pregnant women. What, if any, role estrogen or other hormones play in the disruption of autoregulation during preeclampsia has yet to be determined. Regardless, it is important to remember that the vasculature changes even in normal pregnancy.

Fortunately, cortical blindness due to preeclampsia/eclampsia is almost always a transient phenomenon with reports of blindness lasting 4 hours to 8 days (5, 10, 11, 12, 16). If the blindness is not transient, there should be suspicion of other disease processes. The management of preeclamptic/eclamptic women with cortical blindness is the same as in women without blindness (5). Retinal pigment epithelial lesions and serous retinal detachments have been reported to resolve within 3 weeks in approximately 80% and 98%, respectively, of women with severe preeclampsia or eclampsia (4) (Table 2). Because ophthalmic changes in pregnant patients may herald the rapid onset and progression of preeclampsia, ophthalmologists should be aware that immediate obstetrical referral is indicated for pregnant patients presenting with retinal or choroidal vascular abnormalities (26).

DIABETES

Diabetes is the leading cause of new cases of blindness in United States adults between the ages of 20 and 74 (27). The incidence of diabetes has been found to be higher in women than men (28), and the age-adjusted female to male ratio of blindness due to diabetes is 1.4:1 (27). In 1997 alone, an estimate $98 billion was spent in the United States on medical care because of diabetes (29).

Multiple studies have demonstrated that there is a worsening of retinopathy in diabetics during the course of pregnancy (30–34), but gestational diabetes does not seem to increase the risk of diabetic retinopathy (35). There is an association of increased risk of fetal loss and

TABLE 2 **Ocular disturbances in preeclampsia/eclampsia**

Disturbance	Prognosis
Retinal pigment epithelial lesion	Usually resolves within 3 weeks postpartum
Serous retinal detachment	Usually resolves within 3 weeks postpartum Results in scarring in only a small number of patients
Cortical blindness	Almost always a transient phenomenon lasting 4 hours to 8 days Resolves with resolution of preeclampsia/eclampsia

obstetric complications with worsening of retinopathy and particularly with the development of proliferative retinopathy (32, 35–37) (Table 3). Long-term studies suggest that retinopathy does not seem to be more severe in parous versus nulligravid diabetic women (30, 34, 38–43). Increasing parity does not increase the risk of worse retinopathy (40, 41), and retinopathy may even be less severe in women with two or more pregnancies (40). The progression of retinopathy during pregnancy is influenced strongly by coexisting hypertension and preeclampsia (31, 44, 45) and is directly related to the severity of preexisting retinopathy (33, 46–49). Furthermore, the progression of preexisting retinopathy and the onset of proliferative diabetic retinopathy are influenced strongly by the duration of diabetes before conception (33, 35, 41, 46, 48, 50). The baseline severity of retinopathy before conception may be a more significant risk factor for the progression of retinopathy; however, duration of diabetes before conception seems to hold more prognostic significance for the development of proliferative retinopathy during pregnancy (46). A prospective cohort study of 155 diabetic women (the Diabetes in Early Pregnancy Study) found that retinopathy progressed to proliferative stages in 18% of patients with less than 15 years of diabetes and in 39% of women with more than 15 years of diabetes (46).

Although tight glycemic control of blood sugars during pregnancy is associated with a decreased risk of fetal macrosomia and congenital malformations (51–54), long-term control of blood sugar improves the course of retinopathy (55). Several studies have indicated that worsening of retinopathy is directly associated with poor glycemic control before conception and during pregnancy (31, 44, 46, 50, 56). The Diabetes in Early Pregnancy study (46) found that women with a baseline glycosylated hemoglobin level greater than 8.05% had an odds ratio of 2.7 (95% confidence interval (CI) was equal to 1.1–7.2) of worsening retinopathy when compared with women with baseline hemoglobin levels less than 6.05%. This is confounded by the fact that transient worsening of diabetic retinopathy is correlated with rapid glycemic control in early pregnancy (30, 44–46, 56). Such a phenomenon used to be attributed to the combination of abrupt control of blood sugars plus pregnancy, but rapid glycemic control is now known to be an independent risk factor (30). Interestingly, transient worsening of retinopathy with rapid glycemic control also has been demonstrated in nonpregnant patients (57).

To reduce the progression of retinopathy during pregnancy, blood sugars should be well controlled before conception (58). The progression of diabetic retinopathy may be worse in pregnant patients whose proliferative retinopathy was not treated with photocoagulation before conception (33); therefore, appropriate treatment of preexisting proliferative retinopathy also should occur before pregnancy (33, 58). Proliferative diabetic retinopathy may be treated appropriately using laser photocoagulation in pregnant patients (33, 59), but reversal of pregnancy-induced changes in retinopathy are common postpartum (30, 32, 42, 43, 45, 47). Current recommendations call for a baseline comprehensive dilated eye examination before conception and the anticipation of follow-up ophthalmologic examination during pregnancy (58) (Table 4). Because the adverse effects of pregnancy persist over the first year postpartum, patients should continue to be monitored by an ophthalmologist for at least 1 year after delivery (30). The necessity of intensive retinal surveillance in patients without poor glycemic control and/or retinopathy is controversial (60). Recommendations for follow-up may need to be based on the severity of retinopathy at the time of conception (1, 2, 49).

TABLE 3 **Risk factors for worsening of diabetic retinopathy during pregnancy**

1. Coexisting hypertension or preeclampsia
2. Severity of retinopathy before conception
3. Duration of diabetes before conception
4. Poor glycemic control before conception
5. Rapid institution of glycemic control

REFRACTIVE EYE SURGERY

Although there are few published articles concerning the results of refractive surgery in women before, during, or after pregnancy, pregnancy is considered by most to be a contraindication to photorefractive keratectomy (PRK) and laser *in situ* keratomileusis

TABLE 4 **Recommendations for diabetic women considering pregnancy or who are pregnant**

1. Glucose should be well controlled before conception.
2. All diabetic women should see an ophthalmologist before or shortly after becoming pregnant.
3. If it is indicated, photocoagulation should be carried out before conception.
4. Proliferative diabetic retinopathy can be treated with photocoagulation during pregnancy, but reversal of proliferative changes is common postpartum.
5. The surveillance during pregnancy may depend upon baseline severity of retinopathy.
6. All diabetic women should follow-up with an ophthalmologist postpartum.

(LASIK) surgeries (61). Sharif (62) studied the refractive results of 18 eyes of 9 women who underwent PRK for the treatment of myopia and became pregnant within a follow-up period of 12 months. He concluded that postoperative pregnancy affected the refractive results in PRK. Twelve (6 patients) of 18 eyes had myopic regression. The 6 eyes in 3 women who had stable refractions became pregnant at least 5 months postoperatively. Furthermore, Starr (63) reported a case of overcorrection in a patient who became pregnant shortly before or after PRK, followed by spontaneous abortion and complete reversal of the overcorrection.

On the other hand, Hefetz et al. (64) concluded pregnancy and labor probably had no effect on refractive results after PRK. The authors were able to document stable refractions in six of eight pregnant patients undergoing PRK, although myopic regression occurred in the other two patients.

The reports of unstable refractions could be due to changes in corneal thickness and/or wound healing during pregnancy. Weinreb et al. (65) measured the corneal thickness in 89 pregnant women and found an increase by about 3% ($P = .01$) in comparison to the control eyes of 18 nulligravid and 17 postpartum women. The increase was attributed to increased water retention during pregnancy. There was no difference in corneal thickness with gestational stage and between the nulligravid and postpartum subjects. Ziai et al. (66) followed 19 pregnant women and also demonstrated an increase in corneal thickness during pregnancy. Park et al. (67) found no change in corneal thickness throughout pregnancy in 24 women during pregnancy but did find an increase in the corneal curvature during the second and third trimesters. This curvature either resolved postpartum or after the cessation of breast-feeding. Despite a change in curvature, Park et al. (67) were unable to demonstrate a change in refraction with pregnancy. Manges et al. (68) followed 38 nonpregnant and 93 pregnant patients and found that refractive error, corneal curvature, and corneal thickness did not change significantly during pregnancy.

The timing of refractive eye surgery for a patient intending to become pregnant can be a difficult decision. Because of documented changes in corneal curvature that occur during pregnancy, current recommendations are to delay refractive surgery during pregnancy and wait until stability of refraction is documented postpartum (61). If a patient intends to get pregnant within 1 to 2 years of surgery, it is recommended to postpone PRK or LASIK until after pregnancy (69) (Table 5).

TABLE 5 **Recommendations for women considering refractive eye surgery**

1. Candidates should not intend to become pregnant for 1 year after surgery.
2. Candidates must not currently be pregnant.
3. Candidates must have a stable refractive prescription documented postpartum.

CONTACT LENS INTOLERANCE

Despite success with contact lenses previously, many women develop contact lens intolerance while pregnant (65, 67, 70). This is unlikely to be due to an increase in corneal sensitivity. Conversely, corneal sensitivity either does not change (67) or decreases, possibly relating to water retention (70, 71). The intolerance may actually be due to an increase in either corneal curvature or thickness associated with pregnancy (65, 67, 70), and pregnant women should delay fitting new contact lenses until several weeks postpartum (65, 70). Because stable refractions have been documented for most women during pregnancy (67, 68), pregnancy is not a contraindication to prescribing corrective lenses.

GLAUCOMA

The exact effects of pregnancy on the intraocular eye pressure in glaucoma are not entirely understood. Interestingly, pregnancy has been associated with about a 10% decrease in intraocular pressure in healthy eyes (65). In addition to the decreased intraocular pressure, an increased aqueous outflow capacity has been demonstrated in pregnant patients without glaucoma (66, 72). These changes in aqueous dynamics are consistent with the hypothesis that excess progesterone during pregnancy blocks the ocular hypertensive effects of endogenous corticosteroids (66).

There is little information concerning the safety of glaucoma medications during pregnancy (73, 74); yet, one must be cognizant of the side effect profile and potential teratology of glaucoma medications if a woman with glaucoma becomes pregnant or anticipates a pregnancy. Most glaucoma medications are in the pregnancy category C or B; however, the cholinesterase inhibitors belong to the pregnancy category X (73). Although it is not known if most of the glaucoma medications are excreted into human breast milk (73, 74), several do have the potential (74). In fact, timolol (75, 76) and acetazolamide (77) have been found in human breast milk, but both are considered compatible with breast-feeding (78). A

woman who is breast-feeding should discuss an appropriate regimen with her ophthalmologist and be counseled about the risk of passing glaucoma medications to her infant while nursing. If a woman with severe glaucoma wishes to decrease the potential risk of medications, she may be a candidate for glaucoma surgery (74). Additionally, caution should be used when prostaglandin E_2 is used to induce cervical ripening in women with glaucoma or high intraocular pressure (79).

CONCLUSION

Preeclampsia and eclampsia are associated with an increased incidence of a multitude of visual disturbances, including serous retinal detachment and blindness. Consequently, the obstetrician should perform a fundus examination on all preeclamptic and eclamptic patients. The pathophysiologic mechanisms undermining these disturbances are still being elucidated; however, vascular abnormalities play a role. Fortunately, retinal lesions and blindness often resolve postpartum. Traditionally, medications are not used to lower intraocular pressure in systemic hypertensive diseases.

All diabetic women should see an ophthalmologist before or shortly after becoming pregnant. Poor glycemic control before pregnancy is associated with worsening of retinopathy, and good glycemic control should occur before conception. Coexisting preeclampsia and hypertension also offer a worse prognosis. Long-term studies suggest that retinopathy is no worse in parous versus nulliparous women, and pregnancy-induced retinopathy often regresses postpartum. Proliferative retinopathy can be treated using lasers during pregnancy, but results are better if appropriate treatment of retinopathy occurs before pregnancy.

The results of refractive eye surgery shortly before, during, or after pregnancy cannot adequately be predicted. This elective surgery should be postponed until a stable refraction is obtained postpartum. Because contact lens intolerance is common during pregnancy, it may be wise to avoid prescribing new contact lenses until after delivery. Healthy women may demonstrate a change in corneal curvature and a decrease in intraocular pressure during pregnancy. Glaucoma patients who are pregnant or nursing should be counseled about the potential risks of glaucoma medications to fetuses/infants.

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