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Review Article

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Ocular Changes in Pregnancy

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Abstract

Pregnancy is known to influence the eyes in many ways. The distinction of these ocular changes in pregnancy as benign or pathological is important. Exact diagnosis and appropriate treatment of these conditions can minimise the ocular morbidity. Pre-existing pathologies of the eye like diabetic retinopathy and glaucoma can also worsen or improve during pregnancy. Regular perinatal eye screening can assure healthy status of the eyes. The benefits of ocular treatment to the mother need to be weighed against the potential harm to the fetus. We have thus reviewed the common conditions affecting the eyes during the pregnancy that an obstetrician and ophthalmologist should know for timely referral and management.

Keywords: Pregnancy; Eye; Eye Diseases in Pregnancy; Diabetes; Glaucoma; Ocular Changes; Treatment of Eye during Pregnancy

Introduction

Hormonal interactions in pregnancy influence all the systems of the body including eyes. The ocular changes can be physiological or pathological. The pathological changes can be new onset ocular conditions, alterations in existing ocular pathologies or ocular sequelae of systemic diseases [1].

Although beneficial for pregnant women with glaucoma and uveitis, it can worsen pre-existing diabetic retinopathy. Majority of them are transient in nature and resolve postpartum but can be permanent also. The diagnoses, monitoring and treatment of these ocular changes are reviewed in this article to assist the clinician in distinguishing between benign and pathological conditions.

Physiological changes in pregnancy

Eyelids

Chloasma or melasma, is seen as hypermelanosis of eyelids and cheeks during pregnancy and resolves postpartum [2]. It is a result of increased estrogen, progesterone and melanocyte-stimulating hormone [3]. Unilateral ptosis can occur in pregnancy because of hormonal effects on levator aponeurosis and fluid retention, which resolves postpartum [4]. A pre-existing undiagnosed prolactinoma can enlarge during pregnancy causing ocular symptoms like ptosis [5].

Conjunctiva

Conjunctival capillaries decrease and granularity of the venules increases which resolves post-partum [6].

Cornea

Corneal curvature and thickness increases in the second and third trimesters of pregnancy. It is most likely due to water retention and usually returns to normal with delivery [7]. Thus refraction is unstable during pregnancy and new eyeglass or contact lens prescription should be avoided during pregnancy. Also, refractive surgery is better postponed till stability is achieved. Some studies, however, have demonstrated progression of keratoconus during pregnancy which persists even after delivery [8]. Corneal sensitivity decreases in pregnancy. Pregnancy causes dry eyes due to increased immune reaction leading to damage to lacrimal acinar cells by prolactin, transforming growth factor beta-1 and epidermal growth factor. Contact lens intolerance has also been reported, so it is advisable to delay contact lens wear until several weeks post-partum [9]. Krukenberg spindles are seen early in pregnancy most likely due to low progesterone levels and disappear by the third trimester when there is an increase in progesterone levels and aqueous outflow [10].

Crystalline lens

Water retention can result in development or exacerbation of cataracts during pregnancy. Increased lens curvature leads to a myopic shift. Temporary loss of accommodation during pregnancy and post-natal period is reported [11].

Retina and choroid

Normal pregnancy causes no physiological changes in the retinal arterioles, venules and capillary bed [11].

Intraocular pressure (IOP)

IOP decreases by 2 - 3 mmHg during pregnancy mainly under the influence of progesterone hormone [12]. Various mechanisms have been proposed to explain pregnancy-related IOP reduction, including increased aqueous outflow, lower episcleral venous pressure due to decreased systemic vascular resistance, lower scleral rigidity as a result of increased tissue elasticity, and general acidosis during pregnancy [13].

Effects of pregnancy on pre-existing ocular conditions

Glaucoma

Pregnant women with existing glaucoma may show improvement due to the physiological reduction in IOP and the increased central corneal thickness. This has a benefit in helping to avoid use of anti-glaucoma medication which are mostly category C drugs and have potential to cause teratogenicity. Laser trabeculoplasty, cyclophotocoagulation, trabeculectomy, or shunt tube surgery can benefit patients with glaucoma planning pregnancy [14]. Acute angle-closure glaucoma has been reported during labour [15].

Diabetic retinopathy

It is the most common ocular condition modified by pregnancy and is an independent risk factor for development and progression [16]. Factors associated with progression of retinopathy during pregnancy are hyperglycemia, duration of diabetes before pregnancy, degree of retinopathy in the beginning of pregnancy, glycemic control and comorbid hypertension [17]. It is postulated that pregnancy leads to activation of certain immune system components linked to pathogenesis of diabetic retinopathy (DR) [18].

American Academy of Ophthalmology's preferred practice pattern suggests that diabetic women have an eye examination before conception and then during first trimester of pregnancy, and the follow-up examinations depend on the initial degree of retinopathy [19].

Gestational diabetes carries a low risk of progressing to retinopathy. Previous studies showed that only 10% of mothers without DR at the beginning of pregnancy developed non-proliferative diabetic retinopathy (NPDR) and less than 0.2% of those patients developed proliferative diabetic retinopathy (PDR). Thus, in the absence of visual symptoms, a baseline examination is sufficient in first trimester.

In patients with NPDR, 50% showed progression in retinopathy, that regressed in the third trimester and postpartum [20]. About 5 - 20% of severe NPDR cases progressed to PDR of which up to 45% of their disease can progress during pregnancy [21]. The standard treatment of DR, panretinal photocoagulation (PRP), can be safely performed during pregnancy [22]. In patients with PDR and severe NPDR, planning PRP before pregnancy could reduce the risk of progression by 50% [20,23].

Pregnant patients with PDR whose disease has regressed in the third trimester and postpartum period are recommended to have monthly examinations. Patients with no DR to moderate NPDR should be re-examined every 3 to 12 months, and those with severe NPDR or worse should be re-examined every one to three months [23].

Diabetic macular edema, seen with proteinuria or hypertension, can worsen during pregnancy. It spontaneously resolves postpartum, but can remain in some cases and cause long-term visual loss [9]. Clinically significant disease can be treated with laser therapy [20].

Anti-vascular endothelial growth factor (anti-VEGF) injection is the accepted treatment modality for retinal vascular disorders and neovascularization in PDR in patients of childbearing age [24]. It is normally considered safer during pregnancy. However, few studies have reported miscarriage and complication [25]. Bevacizumab and ranibizumab are category C drugs and theoretically can affect placental vasculature. Bevacizumab is preferred over Ranibizumab as its high molecular weight can prevent it from crossing the placenta. Thus, the decision to treat with antiVEGF agents needs to be made individually on a case based approach by a well informed patient and her physician with carefully monitored pregnancy.

Uveal inflammatory disorders

Non-infectious uveitis has been seen to improve in pregnancy, especially from the second trimester onwards, with the third trimester associated with the lowest activity, probably due to immunosuppressive effects and high levels of corticosteroids present. However, there is a risk of exacerbation postpartum. Ankylosing spondylitis associated anterior uveitis can be more common in the early postpartum period [13]. Postpartum endogenous endophthalmitis secondary to *Candida*, presumed to be due to intravascular dissemination around the time of delivery, has been reported [26].

Posterior scleritis worsens and recurrence increases during pregnancy [27]. Although the standard treatment is oral steroids, posterior sub-Tenon's triamcinolone injection is recommended for pregnant patients [13]. Choroidal neovascularization (CNV) can develop during pregnancy in case of myopia, punctate inner choroidopathy (PIC), presumed ocular histoplasmosis syndrome (POHS) or idiopathic [24,25].

Vogt-Koyanagi-Harada syndrome has been reported to regress and in some cases completely resolve during pregnancy and the postpartum period [28].

The improvements in these chronic sight threatening uveitic ailments during pregnancy can help pregnant women in reducing or avoiding systemic treatment related adverse events for which data is lacking.

Central serous chorioretinopathy

The risk of CSCR is increased in pregnancy by 9 times, due to the high levels of circulating corticosteroids, mostly seen in third trimester [29]. Fibrinous subretinal exudates are more commonly reported in a pregnant female with CSCR than a non-pregnant patient with CSCR [30]. Spontaneous regression is observed at the end of pregnancy or after birth; however, there may be a tendency for recurrence in the same eye in subsequent pregnancies [30]. Laser is reserved only for selected cases.

Optic neuritis

Incidence of optic neuritis decreases during pregnancy like other inflammatory conditions. It has been reported with hyperemesis gravidarum. The relapses decrease in third trimester and increase early postpartum in multiple sclerosis [31]. Multiple sclerosis can present for the first time during pregnancy [32].

Ocular toxoplasmosis

A primary infection or reactivation of latent ocular toxoplasmosis during pregnancy causes decreased vision and floaters. Women with active infection during pregnancy should be monitored every three months [33]. The risk of transmission to the fetus is frequent in the third trimester due to the greatest contact between maternal and fetal circulation. The fetal damage, however, is more severe if the infection is acquired during first trimester with decrease in the risk in second and third trimester. Spiramycin is the drug of choice during pregnancy. Systemic toxicity can be avoided by intravitreal injection of clindamycin and dexamethasone [34].

Ocular tumors

Choroidal haemangiomas have been reported to undergo rapid growth during pregnancy and regress postpartum [10]. It was believed that uveal melanoma can present for the first time or grow rapidly during pregnancy [35], however recent studies rule out the hormonal influence for this [36]. No evidence suggests for termination of pregnancy for a woman with uveal melanoma to avoid metastasis to the fetus [10].

Ocular pathology emerging with pregnancy

Pre-eclampsia and eclampsia

About 5% of pregnant women develop preeclampsia and a one third of them have ocular manifestations.[26] Most frequent complaint is blurred vision. Photopsia, scotoma, and diplopia are also reported [37]. The degree of retinopathy is proportional to the severity

of preeclampsia. The possible underlying mechanisms could be: hypoperfusion, ischemia, endothelial damage, hormonal changes and coexisting systemic vascular disease. The clinical findings are similar to hypertensive retinopathy with focal and generalised arteriolar attenuation. More severe involvement includes retinal edema, cotton wool spots, hemorrhages, retinal nerve fibre layer infarction and even neovascularisation causing vitreous hemorrhage. Optic nerve in preeclampsia can manifest papilledema, ischemic optic neuropathy and atrophy. Exudative retinal detachment is seen in 1% of preeclamptic patients and 10% of eclamptic patients [37]. Most of these findings return to normal following the resolution of preeclampsia [38]. There is a reported case of cortical blindness associated with pre-eclampsia [12].

Occlusive vascular disorders

Pregnancy is a hypercoagulable state, pregnancy related central and branch retinal arterial occlusions are rarely reported and retinal vein occlusions are even rarer.

Purtscher-like retinopathy, characterised by extensive cotton-wool spots with or without retinal hemorrhages and severe bilateral visual loss, has been reported in the immediate post-partum period. Serous retinal detachment, vitreous hemorrhage, central retinal vein occlusion and Purtscher-like retinopathy have been reported in patients with HELLP syndrome [39].

Anti-phospholipid syndrome, an autoimmune disorder, involves both the anterior and posterior segment of the eye characterised by episcleritis, iritis, conjunctival telangiectasia or conjunctival microaneurysms, vitritis, retinal detachment, retinal hemorrhages, cotton wool spots, central serous type chorioretinopathy, posterior scleritis, branch or central retinal vein occlusion, bilateral choroidal infarction, cilioretinal artery occlusion, and venous tortuosity [40].

Disseminated Intravascular Coagulation (DIC), an acquired disorder of systemic intravascular activation of coagulation, frequently involves the choroid. Occlusion of the choriocapillaris by a thrombus leads to disruption of the overlying retinal pigment epithelium, causing serous retinal detachment [41]. Even though the serous detachment resolves, the pigment epithelial changes tend to persist.

Thrombotic thrombocytopenic purpura is a rare disease entity with ocular sequelae in 10% patients. Retinal haemorrhages, exudates, arteriolar narrowing, optic atrophy and serous retinal detachment are known fundus findings. Subconjunctival haemorrhage, extraocular muscle paresis, scotoma, anisocoria and homonymous hemianopia are also reported [42].

Graves' disease

It is the most common cause of hyperthyroidism in pregnancy and an important cause of unilateral and bilateral proptosis. It exacerbates in the first trimester, remits in the second and third trimesters and relapses postpartum [9]. It is characterised by eye stare, eyelid lag, proptosis and extraocular muscle palsy [43]. Mild cases can be observed, while propylthiouracil is the drug of choice for moderate to severe cases in pregnancy [44].

Idiopathic intracranial hypertension

It is common in the first trimester of pregnancy and manifests as visual obscuration, diplopia, scotomata, photopsias, pulsatile tinnitus and retrobulbar pain [45]. Papilledema is typically bilateral but may be unilateral or even absent in some cases [45]. Treatment is observation and weight reduction. Acetazolamide is contraindicated in pregnancy.

Pituitary tumours

A pre-existing pituitary gland tumor shows accelerated growth during pregnancy possibly due to the angiogenetic effect of estrogen [46]. Meningioma and uveal melanoma are the other most common tumors.[35] Pituitary growth of adenomas manifests as decrease in visual acuity, visual field changes mostly bitemporal defects and diplopia. Magnetic resonance imaging is diagnostic in such cases and requires monthly ophthalmologic examination and visual field monitoring. Bromocriptine is a safer treatment option in pregnant women with prolactinomas.

Sheehan syndrome

Also known as pituitary apoplexy, is an enlargement of pituitary gland due to infarction and severe postpartum hemorrhage in pituitary adenoma. It is a vision-threatening condition manifesting as visual field loss (bitemporal superior quadrant), headache and ophthalmoplegia. Ptosis, diplopia and mydriasis can occur if 3rd, 4th and 6th cranial nerves are compressed in the cavernous sinus. Involvement of the sympathetic nerve fibres causes Horner's syndrome [47].

Use of ocular medication during pregnancy

In general, lowest possible dose should be prescribed to limit

systemic absorption and avoid toxicity. Punctual occlusion and wiping away excess eyedrops after administration can further limit systemic absorption. The precise effect of ocular medication on pregnancy and lactation needs further research [48].

Fluorescein crosses the placenta while indocyanine green does not but both are category C drugs. Cycloplegics like tropicamide and cyclopentolate are also category C drugs. Systemic use of atropine, homatropine and phenylephrine has resulted in minor fetal malformations in some cases. Thus, there is a relative contraindication for its ocular use [49]. It is better to avoid its usage in the first trimester even for the purpose of examination.

Erythromycin, ophthalmic tobramycin, ophthalmic gentamicin, polymyxin B, acyclovir and quinolones are safer during pregnancy, while chloramphenicol, neomycin and tetracycline are to be completely avoided [48].

Topical steroid and nonsteroid anti-inflammatory drugs are category C. Topical cyclosporine is in category C. Antihistamines and antiallergy drugs are category C except sodium cromoglycate (category B) [1].

All topical antiglaucoma medications except brimonidine (category B) are category C drugs. Beta blockers can lead to neonatal beta blockade and should be discontinued 2 - 3 days prior to delivery. They should not be used in a lactating mother as concentrated in milk [49]. Systemic and topical carbonic anhydrase inhibitors are contraindicated in pregnancy and lactation due to teratogenicity [50].

Miotic drugs appear to be safer during pregnancy. Prostaglandin use can lead to early delivery or miscarriage. Brimonidine, an alpha 2 agonist, although in category B carries the risk of apnea and bradycardia in the newborn, hence should be avoided during lactation [50].

Lignocaine, a category B drug, is the safest anaesthetic for pregnant women undergoing ocular surgery.[1] Bupivacaine, a category C drug, can cause bradycardia in the fetus, hence not recommended. Proparacaine hydrochloride, a topical anaesthetic, is also in category C [1].

Conclusion

Pregnancy is a unique health condition that necessitates consideration in any health issues affecting women. Ophthalmologists need to be aware of the various physiological and pathological conditions affecting the eye that can influence the outcome.

Conflict of Interest

Nil.

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