

REVIEW ARTICLE

A Review of the Changes in the Ophthalmic and Visual System in Pregnancy

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ABSTRACT

Pregnancy is often associated with ocular changes which may be more commonly transient but occasionally, permanent. It may be associated with the development of new ocular conditions, or can exacerbate pre-existing conditions. The ocular effects of pregnancy may be physiological or pathological or may be modifications of pre-existing conditions. Adnexial changes include chloasma, spider angiomas and ptosis. Anterior segment changes include a decrease in conjunctival capillaries and an increase in the granularity of conjunctival venules and in corneal curvature, changes in corneal thickness, refractive index, accommodation and refractive errors, and a decrease in intraocular pressure. Posterior segment changes include worsening of diabetic retinopathy, central serous chorioretinopathy, increased risk of peripheral vitreochorioretinal dystrophies and retinal detachment, and a beneficial effect on non-infectious uveitis. Systemic disorders of importance include preeclampsia, Graves disease and multiple sclerosis. Intracranial disorders with ocular effects in pregnancy include Pseudotumor cerebri, prolactinomas and Sheehan's syndrome (*Afr J Reprod Health* 2008; 12[3]:185-196).

RÉSUMÉ

Examen des changements dans la grossesse ophtalmique et du système visuel La grossesse est souvent associée aux changements oculaires qui peuvent être plus généralement la coupure, mais de temps en temps, permanents. Il peut être associé au développement de nouvelles conditions oculaires, ou peut renforcer des conditions préexistantes. Les effets oculaires de grossesse peuvent être physiologiques ou pathologiques ou peuvent être les modifications des conditions préexistantes. Les changements annexais incluent chloasma, des angiomes d'araignée et ptose. Des changements de segment antérieurs incluent une diminution dans des capillaires conjonctivales et une augmentation de la granularité de vénales conjonctivales et dans la déviation cornéenne, des changements de l'épaisseur cornéenne, de l'indice de réfraction, et des erreurs réfractions et une diminution dans la pression intraoculaire. Des changements de segment postérieurs incluent la dégradation de rétinopathie diabétique, chorioretinopathie séreuse central, le risque accru du périphérique vitreochorioretinal des dystrophies et le décollement de la rétine et des effets avantageux sur uvéites non contagieuses. Les désordres systémiques d'importance incluent pré éclampsie, la maladie de Tombes et la sclérose en plaques. Des désordres intracrâniens avec des effets oculaires dans la grossesse incluent la Pseudotumeur cérébrale, prolactinomas et le syndrome de Sheehan (*Afr J Reprod Health* 2008; 12[3]:185-196).

KEY WORDS: Pregnancy, Ocular changes, Diabetic retinopathy, Preeclampsia

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Introduction

Women undergo a tremendous number of changes, both systemic and ocular, throughout pregnancy. During pregnancy, physiological changes occur in the cardiovascular, hormonal, metabolic, haematologic, and immunologic systems.^{1,2} By some of these mechanisms, pregnancy causes changes in the eyes such as deterioration in the background retinopathy in diabetic women, even when good metabolic control is achieved and retinopathy is minimal.^{3,4} Compared with non-diabetic pregnant women, retinal capillary blood flow has been reported to be higher in diabetic women during pregnancy and after delivery.⁵ Together with the hormonal and metabolic changes occurring during pregnancy, hyper-dynamic retinal capillary circulation may contribute to the progression of retinopathy in pregnant diabetic women.⁵ Hormonal changes are among the most prominent systemic changes in pregnant women. The placenta, maternal endocrine glands and the fetal adrenal glands combine their productivity to make a high-powered hormone factory. The immune state is suppressed, leaving the pregnant woman more susceptible to serious immunological disorders.² Visual changes in pregnancy are common, and many are specifically associated with the pregnancy itself.⁶ Pregnancy is often associated with ocular changes, most often transient in nature, though occasionally permanent. It can be associated with development of new conditions, or can exacerbate pre-existing conditions. The ocular effects of

pregnancy may be divided into physiologic changes, pathologic conditions or modifications of pre-existing conditions.⁷ This review gives an overview on the changes that can affect the ocular health and vision of a pregnant woman and during childbirth.

Ocular Adnexia

Chloasma which is also known as **mask of pregnancy** is a hormonally-mediated process, characterized by increased pigmentation around the eyes and cheeks.^{8,9} The pigmentation changes tend to fade slowly postpartum. Spider angiomas, a type of telangetasia, commonly develop during pregnancy on the face and upper body.⁸ All these external changes resolve postpartum.^{2,8,9} Ptosis has been reported to occur during and after normal pregnancy and it is usually unilateral.⁹ The mechanism is thought to be due to defects that develop in the levator aponeurosis from fluid, hormonal, and other changes from the stress of labour and delivery.⁹

Anterior Segment of the Eye Conjunctiva

A decrease in the conjunctival capillaries and an increase in the granularity of conjunctival venules have been reported to occur and are reversible postpartum.⁹

Tear film

Pregnancy induced dry eye syndrome may occur due to disrupted lacrimal acinar cells.¹⁰ Pregnancy can trigger alterations of lacrimal gland

growth factor expression and re-distribution of lymphocytes from periductal foci to interacinar sites and enhanced immuno-reactivity of prolactin, TGF-beta1, and EGF in ductal cells.¹¹

Cornea

Many women develop contact lens intolerance while pregnant even when they fit comfortably before pregnancy.^{2,12} In a study of corneal curvature in pregnant women there was a statistically significant increase in corneal curvature during the second and third trimester which resolved postpartum or after the cessation of breastfeeding.¹² Pregnancy is associated with changes in corneal sensitivity and thickness.^{2,13,14} A measurable but slight increase in corneal thickness due to edema occurs during pregnancy. Corneal sensitivity tends to decrease, with the largest changes late in pregnancy.¹⁴ Due to variations in thickness; the refractive index of the cornea may be altered. It is thus advisable to postpone changes in prescription and fitting of contact lenses until several weeks postpartum.

Newly developed Krukenberg spindles on the cornea have been observed early in pregnancy and they tend to decrease in size during the third trimester and postpartum. They are not accompanied by other findings of pigment dispersion, such as increased angle pigmentation and iris transillumination defects.¹⁴ The mechanism presumably is related to hormonal changes such as low progesterone levels, however, by the third trimester, an

increase in progesterone and aqueous outflow often result in decreased or absence of Krukenberg spindles.

Accommodation and Refractive Errors

Changes in accommodation and refractive errors have been reported during pregnancy.^{13,15} Transient accommodative loss has been noted both during and after pregnancy. Accommodative insufficiency and paralysis have been documented in association with lactation.¹⁵ 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.⁶

Intraocular Pressure (IOP)

Pregnancy can have beneficial effects on glaucoma.^{2,6,16} Pregnancy is associated with a decreased IOP in healthy eyes,⁶ and in ocular hypertension,¹⁶ and the effects of glaucoma medications on the fetus and breast-fed infant are largely unknown.⁶ In normal subjects, pregnancy decreased IOP by 19.6%. About 35% of total decrease occurred between 12th and 18th weeks of pregnancy.¹⁶ In ocular hypertension, pregnancy decreased IOP by 24.4%. About 61% of total decrease occurred between 24th and 30th weeks of pregnancy.¹⁶ With advancing pregnancy, intraocular pressure decreases. The higher decrease in ocular hypertensive subjects may be due to their higher level of ocular pressure. In ocular hypertensive subjects, pregnancy can decrease IOP up

to a level of normal limit.¹⁶ Various mechanisms have been implicated for this observation. Such mechanisms include an increase in aqueous outflow; a decrease in systemic vascular resistance, leading to decreased episcleral venous pressure; generalized increased tissue elasticity, leading to decreased scleral rigidity; and generalized acidosis during pregnancy.

Posterior Segment Disorders

Diabetic Retinopathy: Pregnancy can worsen preexisting diabetic retinopathy.¹⁷⁻²⁴ Diabetic changes that occur during pregnancy are similar to the findings in non pregnant diabetic patients and in males. However, pregnancy in diabetic patients with good metabolic control doesn't seem to be a risk factor for developing vascular complications. These complications are still strongly correlated with duration of diabetes.²⁵

There is no difference in the grading procedures. Gestational diabetes (diabetes mellitus that occurs during pregnancy) has not been associated with the development of retinopathy.²⁴ Varying degrees of progression of diabetic retinopathy have been reported. In one report, progression of the retinopathy occurred in 77.5% of the patients who presented with diabetic retinopathy at conception; proliferative diabetic retinopathy occurred in 22.5%.¹⁷ Only 26% of the patients who started the pregnancy without diabetic retinopathy had some progression of the retinopathy.¹⁷ In another report, progression of retinopathy in pregnancy

was uncommon (5.0% pregnancies) but was significantly more common in women with duration of diabetes > 10 years and in women with moderate to severe retinopathy at baseline.¹⁹ Laser therapy was needed in 2.2% pregnancies, which is much lower than that reported in earlier studies.¹⁹ Yet in another report, worsening of initial retinal lesions was observed in 16% of the pregnant group compared to only 6% of the control.²⁰ The difference between the two groups was statistically significant. Argon laser panretinal photocoagulation of pre-proliferative and proliferative DR resulted in no subsequent DR-induced complications.²⁰

Risk factors associated with progression of diabetic retinopathy in pregnancy include duration of diabetes^{20,25} and coexistence of hypertensive disorders.¹⁸ In a study of the risk factors for progression of diabetic retinopathy,¹⁷ it was reported that duration of diabetes was longer in the progressive group compared with the non-progressive group. The glycohemoglobin was higher in the progressive group than in the non-progressive group at each time point, but only in the third trimester was the difference statistically significant. The hemoglobin level was lower in the progressive group than in the non-progressive group. The systolic blood pressure was higher in the progressive group.¹⁷ In another report,²⁶ using logistic regression to control for covariates, ocular perfusion pressure was significantly associated only with incidence of retinopathy in younger-onset

persons. The odds ratio for a 10-mmHg increase in ocular perfusion pressure was 2.13 (95% confidence interval, 1.30-3.50). Also, myopia was protective for progression to proliferative diabetic retinopathy in younger-onset persons. These results suggest that pressure phenomena may be related to the development of retinopathy in younger-onset persons. This would have implications for treatments affecting both IOP and blood pressure.²⁶

Sight-threatening diabetic retinopathy in pregnancy is a rare disease, but it can have devastating consequences for mother and child.²⁷ Laser photocoagulation should be considered for pregnant women with severe preproliferative diabetic retinopathy. Proliferative diabetic retinopathy may not regress postpartum. Close follow-up should be extended in the postpartum period in this group of patients until the retinopathy is stabilized. The presence of combined rhegmatogenous and tractional retinal detachment and neovascular glaucoma has been reported to be associated with poor outcome.²⁷

Central Serous Chorioretinopathy: This is a macular disorder characterized by a localized serous retinal detachment. It most commonly affects young middle-aged adults aged 20 to 45 years. It is usually more common in men more than women at a ratio of 10:1.²⁸ Pregnancy is considered a risk factor for the development of central serous chorioretinopathy.^{13,29} There may be no racial predominance in the development of central serous chorioretinopathy in

pregnancy.²⁸ Central serous chorioretinopathy in pregnant woman is often associated with subretinal exudation which is probably fibrinous in nature.^{28,30} Subretinal fibrinous exudates have been seen in 90% of the patients, compared with fewer than 20% of patients in typical (non-pregnant) central serous chorioretinopathy.²⁸ The affection resolves spontaneously at the end of pregnancy or after delivery, but may recur in the context or outside of subsequent pregnancy.³⁰ The special conditions of pregnancy, including haemodynamic, biological and psychological alterations may lead susceptible women to develop central serous chorioretinopathy.³⁰

Peripheral Vitreochorioretinal Dystrophies (PVC RD): Dynamic observations of 86 pregnant women with peripheral vitreochorioretinal dystrophies (121 eyes) showed that the condition progressed during pregnancy in 33.8% cases.³¹ Decrease of ocular haemodynamics and scleral rigidity were characteristic of pregnancy.³¹ The highest incidence of PVC RD progress was observed in pregnant women with the hypokinetic type of systemic haemodynamics.³¹

Rhegmatogenous Retinal Detachment: Pregnant women who have high myopia, a history of retinal detachment or retinal holes, or have known lattice degeneration are frequently referred to an ophthalmologist for advice concerning the management of pregnancy and labor, i.e. whether a spontaneous vaginal delivery can be allowed and whether

prophylaxis for high-risk retinal pathology is indicated.³² Many obstetricians still believe that pregnant women with ocular abnormalities predisposing to rhegmatogenous retinal detachment should have an instrumental delivery, and a few even advocate Caesarian section. It has been shown that prenatal treatment of asymptomatic retinal pathology is not indicated and that spontaneous vaginal delivery may be allowed to take place in women with high-risk retinal pathology.³²

Macular Edema: Macular edema with and without proliferative retinopathy may also occur during pregnancy. It may develop or worsen during pregnancy. It has been shown that macular edema often is linked in pregnant women with diabetes who also demonstrate proteinuria and hypertension. Studies have shown that some cases have resolved spontaneously postpartum but it may persist in others, causing long-term visual loss.³³

Uveitis: Uveitis refers to inflammation of the uveal tract, comprising the iris, ciliary body and the choroid. It has been reported that pregnancy is associated with lower numbers of flare-ups of non-infectious uveitis compared to the non-pregnant state.³⁴ If flare-ups do occur during pregnancy, they happen predominantly in the first trimester. Specific causes of non-infectious uveitis showing beneficial effects of pregnancy include Vogt-Koyanagi-Harada syndrome, idiopathic uveitis and Behçet's disease.^{35,36} Many of these women will experience a rebound in activity within 6

months of delivery.³⁶ It is considered that the increase of intrinsic hormone, especially corticosteroid, and some other factors with pregnancy may give the suppressive influence on uveitis.³⁵

Toxoplasmosis: Toxoplasmosis is a parasitic zoonosis that occurs worldwide and is an important cause of blindness.³⁷ The infection is naturally acquired by the ingestion of oocysts excreted by infested cats or by ingestion of tissue cysts in undercooked or raw meat. Primary infection during pregnancy may result in a congenital infection. Latent ocular toxoplasmosis may reactivate during pregnancy in the mother. Toxoplasmic retinochoroiditis is the most common cause of posterior uveitis in immunocompetent patients.^{37,38} In adults decreased vision and floaters are most frequently reported. Active toxoplasmic retinochoroiditis typically presents as grey-white retinal necrosis with choroiditis, vasculitis and vitritis. However, atypical presentations including neuroretinitis, papillitis, Fuchs-like anterior uveitis, scleritis and acute retinal necrosis have been described.³⁷ The diagnosis is based on clinical findings and can be supported by the detection of antibodies and *Toxoplasma gondii* DNA using polymerase chain reaction (PCR).^{37,38} Anterior uveitis can occur, with mutton-fat keratic precipitates, fibrin, cells and flare, iris nodules and posterior synechiae.³⁸ It is often fatal in the newborn babies infected by transplacental way, thus, the discovery of a toxoplasmic seroconversion during the follow up of the pregnant women had

posed to the obstetrician some problems in the management.³⁹ The estimated risk of fetal infection ranged between 2 and 10% based on live born children and between 3 and 14% when interrupted pregnancies were included.⁴⁰ Toxoplasmosis therapy includes antimicrobial drugs and corticosteroids. For early maternal infections as for those acquired later, the recommendation is immediate treatment with spiramycin, monthly ultrasound surveillance, amniocentesis and treatment with pyrimethamine and sulphamides if the PCR is positive.⁴⁰ The prognosis for ocular toxoplasmosis is favorable in immunocompetent individuals, as long as the central macula is not directly involved.^{37,38}

Systemic Diseases in Pregnancy Affecting the Ocular System

Hypertensive disorders: The onset of the triad of hypertension, oedema and proteinuria in an otherwise normotensive pregnant woman, is termed pregnancy-induced hypertension (PIH) or preeclampsia. If these changes are associated with seizures, then the disorder is referred to as eclampsia.² another category is “pregnancy-aggravated hypertension,” which is preeclampsia or eclampsia superimposed upon chronic hypertension.⁴¹ Preeclampsia is an obstetric disease of unknown cause that affects approximately 5% of pregnant women. The visual system may be affected with variable intensity.⁴² Visual symptoms are common in patients with pre-eclampsia, and are caused by various underlying

pathological changes in the retina. Blurred vision may be one of these symptoms.⁴³ Retinal detachment in preeclampsia is usually bilateral and serous, and its pathogenesis is related to the choroidal ischemia secondary to an intense arteriolar vasospasm.⁴² In affected eyes, the patients complain of a relative central scotoma. Ophthalmoscopy may show edema in the affected maculae, while a serous neurosensory detachment of the macula, a neurosensory detachment in the papillomacular region or late leakage and subretinal exudates may be detected.⁴³ The majority of patients have complete recovery of vision with clinical management, and surgery is unnecessary.^{42,44}

Cortical blindness is a rare complication of preeclampsia.^{45,46,47} It is usually reversible and most likely due to vasogenic edema rather than vasospasm.⁴⁷ Other ocular pathology seen in preeclampsia include reduced arteriole to venule ratio, acute hypertensive retinopathy, choroidal infarcts, papillophlebitis, retinal artery and vein occlusion, retinal pigment epithelial changes, optic neuritis, optic atrophy, ischemic optic neuropathy, and thrombosis of the central retinal artery.^{48,49,50,51}

Graves Disease: Autoimmune thyroid disease, including Graves' disease and autoimmune thyroiditis, is common in women of childbearing age.⁵² rarely; the fetus can be affected because of transplacental passage of maternal IgG. Graves' disease is the most common

cause of hyperthyroidism in pregnancy. It is an important cause of unilateral and bilateral proptosis. Pregnant women with Graves's orbitopathy are treated in a similar fashion to non-pregnant women. Graves' disease tends to remit late in pregnancy and relapse postpartum.⁵³ the diagnosis of Graves' disease in pregnancy can be complex because of normal gravid physiologic changes in thyroid hormone metabolism.⁵⁴ Mothers with active Graves' disease should be treated with antithyroid drugs, which impact both maternal and fetal thyroid function. Optimally, the lowest possible dose should be used to maintain maternal free thyroxine levels at or just above the upper limit of the normal nonpregnant reference range.⁵⁴ Mild cases may be monitored, but moderate to severe cases must be treated. Thyroid inhibitors such as propylthiouracil, methimazole and carbimazole all cross the placenta and are excreted in breast milk, but the drug of choice in pregnant women is propylthiouracil.⁵³

Multiple sclerosis (MS): This is an important cause of optic neuritis. Multiple sclerosis is the most common chronic disabling neurological disease affecting young women.⁵⁵ paradoxically, our knowledge of the relationship between pregnancy and MS is limited. The influence of pregnancy in multiple sclerosis (MS) has been a matter of controversy for a long time. Women with MS were often discouraged to envisage pregnancy.⁵⁶ However, several conclusions emerge from the literature:^{55,56}

- 1) The rate of relapse in MS decreases

- during pregnancy, and it rises significantly during the first three months post partum before coming back to its level prior to pregnancy.
- 2) Although pregnancy and delivery cause changes of the relapse rate, they have no influence on mid and long term residual disability.
- 3) Epidural analgesia do not seem to have any deleterious effect on the disease.
- 4) Lastly, MS does not seem to influence pregnancy, delivery or the child's health. Pregnancy does not appear to be a period at greater risk for exacerbations but, on the contrary it seems to act, on the whole, as a protective event. These data allow physicians to provide reassuring counseling to women.⁵⁷ Puerperal immune-mediated changes are responsible for activation of optic neuritis associated with relapsing multiple sclerosis.⁵⁸ This may result in acute loss of vision in breastfeeding women and may be the presenting feature of multiple sclerosis.⁵⁹ Multiple sclerosis must be considered as an etiology for acute puerperal lactation-associated blindness when there is no clear anatomic or infectious cause.⁵⁹

Intracranial Conditions in Pregnancy Affecting Vision

Pseudotumor cerebri (PTC): PTC which is also known as Benign Intracranial Hypertension (BIH) is a syndrome characterized by intracranial hypertension and associated with headaches, visual disturbances and papilloedema, but without any identifiable intracranial pathology.⁶⁰ It is a rare disorder occurring in the reproductive age range of females, thus

occurring infrequently in pregnancy.⁶¹ Changes of endocrine status have been found to prevail among aetiological factors, viz. pregnancy, obesity, galactorrhea-amenorrhea, hypothyroidism, ingestion of oral contraceptives.⁶² The patients show signs of intracranial hypertension (headache, vomiting, congested optic discs). The spinal fluid pressure is elevated, with the cellular and protein composition being normal. The condition is marked by benign course and favorable outcome.⁶² Overall, pregnancy outcome does not appear to be adversely affected and the risk of recurrence in subsequent pregnancies does not appear to be increased.⁶¹ Once diagnosed, the decision to treat is based on visual acuity and visual field loss. Medical management and observation are usually effective. Pregnancy is not contraindicated in women with pseudotumor cerebri, and termination of pregnancy is seldom required.^{60,61}

Intracranial Tumors: Prolactinomas are the most common functioning tumors seen in the pregnant patients.⁶³ They may be micro or macro adenomas. Hormone fluctuations during pregnancy can stimulate estrogen receptors on the prolactinoma, leading to tumor enlargement.⁶⁴ Thus, previously asymptomatic pituitary adenomas or micro adenomas may enlarge and result in various ophthalmic symptoms, such as headache, visual field and/or visual acuity loss. For this reason, patients with amenorrhea should be screened to rule out a pituitary mass prior to initiating pro-ovulation medications. Symptomatic

pituitary adenomas may require the combined efforts of an ophthalmologist, obstetrician, neurosurgeon, and endocrinologist to decide upon appropriate medical, surgical, or radiation treatment. In cases of prolactinomas, bromocriptine, a dopamine agonist, can lower prolactin and cause shrinking of the tumor. Bromocriptine is considered safe to use during pregnancy and is not associated with increased risk of spontaneous abortion, congenital malformation or long-term postnatal development.⁶⁵ If the tumor does not respond to drugs, transsphenoidal hypophysectomy is advocated during the second trimester, with delivery taking place in the third trimester.⁶⁴

Sheehan's syndrome: Sheehan's syndrome or pituitary apoplexy occurs as a result of ischemic pituitary necrosis due to severe postpartum hemorrhage. It may be rarely seen without massive bleeding or after normal delivery.⁶⁶ It is a potentially visual-threatening complication of pituitary adenomas because of the sudden increase in pituitary size from infarction or hemorrhage. This condition may present as a sudden onset of headache, visual loss, and/or ophthalmoplegia. It is one of the most common causes of hypopituitarism in developing countries.⁶⁶ Enlargement of pituitary gland, small sella size, disseminated intravascular coagulation and autoimmunity have been suggested to play a role in the pathogenesis of Sheehan's syndrome in women who suffer from severe postpartum

hemorrhage.⁶⁶ The great majority of the patients have empty sella on CT or MRI.

In conclusion, pregnancy may result in several changes affecting all the segments of the eye. Some of these changes may be beneficial while others are not. The majority are however, transient with resolution of symptoms after delivery.

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