

## Eye Changes In Pregnancy: Many Things Can Be Missed

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**Abstract:** The virtue of becoming a mother is God's greatest gift to womankind. However, sometimes the mother has to pay a heavy duty for this privilege. During pregnancy, there are progressive anatomical, physiological, and/or may be even some pathological changes which involve not only the reproductive system but also all other organ systems of the body even including the eyes. Pregnancy can affect the eyes in many ways (i.e. physiological or pathological) which are being described in this article.

### I. Introduction

Pregnancy is a state associated with marked changes in different organ systems of the body (Table 1). These changes, which are a consequence of the hormonal changes during pregnancy (Table 2), result alterations which can have a bearing on both the structure and function of different organ systems. As with all other major organ systems, the eyes and their adnexa too undergo significant changes during pregnancy. These changes are difficult to observe and quantify for a number of reasons. Risks to the fetus preclude any invasive testing to the mother (including tests that might be considered non-invasive in a non-pregnant patient) unless it is clearly indicated for maternal health. Also, diseases affecting women of childbearing age affect pregnant as well as non-pregnant women.

The ocular effects of pregnancy can be divided into three categories though there is some overlap among these categories. Physiological changes of pregnancy are those that one might expect to see in eyes, due to pregnancy itself, and would not be considered pathological. Pathological conditions could develop during pregnancy, which were not evident prior to pregnancy, and might be considered to be caused by or associated with the pregnancy itself. Last but not the least, pre-existing conditions, such as diabetic retinopathy, tumours, and immunologic disorders, may be modified by pregnancy.

#### Physiological ocular changes

Normal pregnancy induces various physiological changes in the eye. The most important changes seen are related to the lids and adnexal tissues, cornea, intraocular pressure (IOP) and visual function.



**Figure 1:** Clinical photograph of face of a pregnant lady showing Chloasma gravidarum

**Lids and adnexal tissues**

Pregnancy can lead to ptosis, which is either due to disinsertion of the aponeurosis of the levator palpebrae superioris (LPS) or due to infiltration of water molecules into the collagen ground substance of LPS and its tendon or possibly both. It responds well to surgical treatment<sup>1</sup>.

**Table 1 : Systemic Changes in Pregenancy**

- |     |  |                  |
|-----|--|------------------|
| 1.  | Weight gain.....   | 11 kg (average)  |
| 2.  | Water retention.....   | 6.5 litres       |
| 3.  | Haematological Changes:  |                  |
|     | Blood volume.....  | increase 30-45%  |
|     | Circulating erythrocytes.....  | increase 20-33%  |
|     | Clotting factors and clotting activity increase  |                  |
|     | Blood viscosity.....   | decrease         |
| 4.  | Cardiovascular Changes :   |                  |
|     | Resting pulse rate.....  | increases        |
|     | Cardiac output.....  | increases        |
|     | Vascular resistance.....   | decrease         |
|     | Arterial blood pressure.....   | decrease         |
|     | Lower limb venous pressure.....  | increases        |
| 5.  | Cutaneous Changes :  |                  |
|     | Cloasma gravidarum or pregnancy mask   |                  |
|     | Striae gravidarum, vascular spider and Palmer erythema   |                  |
| 6.  | Metabolic Changes :  |                  |
|     | Total Metabolism (BMR).....  | increases 30%    |
| 7.  | Respiratory Changes :  |                  |
|     | Respiratory rate/minute.....   | unaffected       |
|     | Vital capacity (ml) .....  | unaffected       |
|     | Tidal volume (ml) .....  | increases 40%    |
|     | Residual volume (ml) .....   | decreases 20%    |
| 8.  | Urinary System :   |                  |
|     | Renal plasma flow.....   | increases 25-50% |
|     | Glomerular filtration rate (GFR).....  | increases 50%    |
| 9.  | Alimentary System :  |                  |
|     | Gums hypertrophied and congested   |                  |
|     | Muscle tone and motility of GI tract....   | decrease         |
|     | Cardiac sphincter.....   | relaxed          |
| 10. | Liver and Gall bladder :   |                  |
|     | All liver functions.....   | decrease         |
|     | Tonicity of gall bladder.....  | decrease         |
| 11. | Nervous System :   |                  |
|     | Some sort of temperamental changes found (i.e. Nausea, Vomiting, Mental irritabilty and Sleeplessness) |                  |
| 12. | Ocular Changes: Given in the test.   |                  |

Skin of the face and also around the eyelids (most often on cheeks) becomes blotchy brown (hypermelanosis) in colour which generally fades slowly postpartum (Figure 1). It is thought to be caused by the elevated levels of melanocyte stimulating hormone (MSH) present from the end of the second month of pregnancy to term, or by the melanocyte stimulating effects of estrogen and progesterone. Spider angiomas are telangiectasias which commonly develop during pregnancy on the face and upper body and are due to increased levels of estrogen hormone<sup>2</sup>.

<b>Table 2: Hormonal changes during pregnancy</b>		
<b>Hormones</b>	<b>changes</b>	<b>function(s)</b>
1. Placental Hormons		
1. Human chorionic gonadotrophin (hCG)	Increase	- Maintains corpus luteum of pregnancy - Acts as LH surrogate
2. Human placental lactogen (HPL)	Increase	- Thyroid stimulating properties - Lactogenic properties - Growth hormone like properties - Also anti-insulin (diabetogenic) action
3. Hypothalamic type releasing hormones		
a. Luteinizing hormone releasing hormone (LHRH)	Increase	- Increase secretion of LH, Thyroxine and corticosteroid
b. Thyrotropin releasing hormone (TRH)	Increase	
c. Corticotropin releasing factor (CRF)	Increase	
4. Somatostatin	Increase	- Growth hormone inhibition
5. Steroid hormone(estrogen and progesterone)	Increase	- Play crucial role in the maintenance of pregnancy - Development and hypertrophy of breasts - Involved in the complex pathway for initiation of labour - Preserves gonadal function by inhibiting cyclic fluctuating activity of to nadotropic-gonadal axis
6. Relaxin	Increase	- Play role in collagen remodelling - Loosens the ligaments of pubic symphysis and softens the cervix which facilitates delivery of fetus.
II. Pituitary hormones		
1. Growth hormone	Increase	- Positive nitrogenous and phosphorous balance (weight gain)
2. Prolactin	Increase	- Increase milk secretion
3. Thyroxine free	Increase	- Net effect is no increase in Thyroxine level
4. Thyroxine binding protein	Increase	
5. Cirulating cortisol	Increase	- Water and salt retention
6. Anti diuretic hormone (ADH)	Increase	- Water and salt retention
7. Oxytocin frequency of	Increase	- Increase force and Uterine contractions during Labour. - Milk ejection reflex

**Intraocular pressure (IOP)**

With rare exceptions, IOP has been reported to decrease during pregnancy in response to increased levels of estrogen, progesterone, hCG and relaxin hormones. Increased facility of outflow has been found in pregnancy and has been thought to be one possible reason for the decreased IOP. It has been postulated that there is increased uveoscleral outflow which possibly has a hormonal basis. A decrease in episcleral venous

pressure reflective of a general decrease of venous pressure in the upper extremities may be an additional cause. Another proposed reason for the decreased IOP is the mild metabolic acidosis of pregnancy. Preexisting glaucoma has been reported to improve during pregnancy with rare exceptions, and it is unusual for glaucoma to be first noted during a pregnancy. Only minor changes in ocular rigidity have been noted during pregnancy which suggests that ocular rigidity changes are not the cause of the decrease in IOP<sup>3</sup>.

### **Corneal and conjunctival changes**

In most pregnant women, corneal sensitivity has been found to be decreased, with most of the changes occurring late in pregnancy. The sensitivity returns to normal level by six to eight weeks postpartum<sup>4</sup>. A measurable, but slight, increase in corneal thickness, thought to be due to edema, has been also found in pregnant women. The amount of increased corneal thickness is unrelated to the degree of sensitivity loss.

Pregnant women may have difficulty with previously comfortable contact lenses and this may be related to increased corneal thickness, alteration in tear composition, or corneal edema. Because a change in corneal thickness changes the refractive index of the cornea to a small extent, one should wait for several weeks postpartum before prescribing a new correction. Kruckenberg spindles have been observed with a higher than expected frequency in pregnant women and have been noted to decrease in size in the third trimester and postpartum. They are generally not accompanied by other evidence increased anterior segment pigmentary dispersion. Hormonal effects are postulated to be the cause of this increased pigmentation, and the increased facility of outflow is suggested as the possible cause of the clearing of pigment late in pregnancy. There may be a granularity in the conjunctival venules towards the end of a normal pregnancy which has been attributed to a gradual reduction in blood flow rate. A mild spasm of conjunctival arterioles may be noted in the third trimester with a decrease in the number of capillaries visualized as the pregnancy proceeds<sup>5</sup>.

### **Visual function changes**

The studies on visual function changes in pregnancy have shown conflicting results. Variable changes in the visual fields have been reported, with some studies finding bitemporal contraction of the visual fields in a large majority of pregnant women, some finding concentric contraction, and some finding no change in most patients. When changes are found, they usually resolved by ten days postpartum. None of the reports mention any subjective complaints by normal pregnant women of visual field changes<sup>6</sup>.

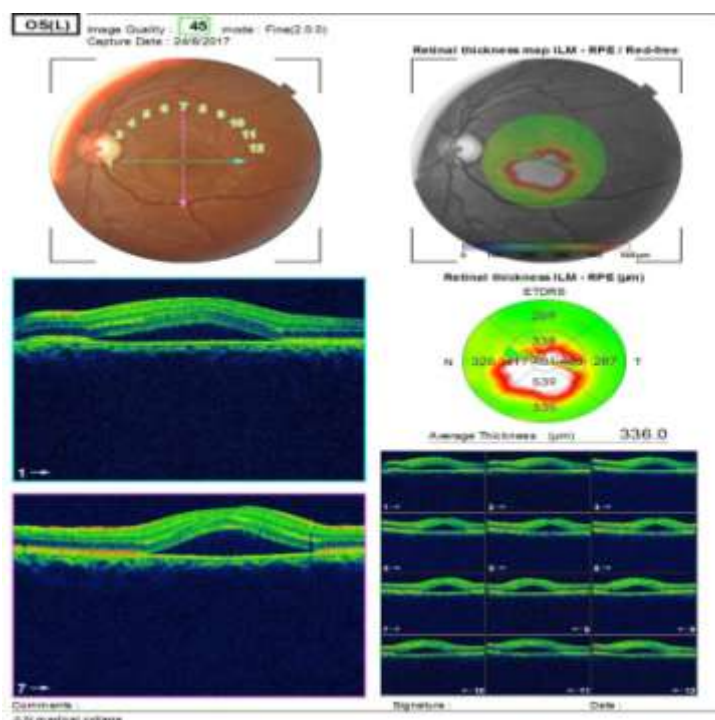
A transient loss of accommodation has been reported during and after pregnancy and accommodative insufficiency and paralysis have been reported in association with lactation.

### **Pathological changes in pregnancy**

The pathological changes are conditions which might be considered to be caused by or associated with the pregnancy itself, but are not evident prior to it. The possible examples of these changes are central serous chorioretinopathy, uveal melanomas, vascular disorders, benign intracranial hypertension (pseudotumour cerebri), coagulation disorders and amniotic fluid embolism.

### **Central serous chorioretinopathy**

Central serous retinopathy (CSR) can develop during the first, second or third trimesters of otherwise normal pregnancies (Figure 2). In all of these cases, symptoms resolve and vision recovers following delivery, with only mottling and clumping of the retinal pigment epithelium as evidence that the event had occurred. Proposed causes for such an association of CSR with pregnancy include hormonal and hemodynamic alterations (increased steroid levels, increase in red blood cell volume and cardiac output, changes in permeability along with decreased colloid osmotic pressure and hypercoagulability)<sup>7</sup>. Since CSR is much more common in males than females, one might not think of a diagnosis of CSR in a pregnant woman, unless one was aware of its possibility.



**Figure 2:** Optical coherence tomography picture of left eye of a pregnant lady showing central serous retinopathy.

### Hypertensive disorders

Pregnancy induced hypertension (PIH) although rarer than in the past, does occur and causes ocular changes that can lead to decreased vision during pregnancy and postpartum. PIH is hypertension occurring during pregnancy in a previously normotensive woman. Also included in this category are preeclampsia, a condition of hypertension, edema, and proteinuria generally presenting after twentieth week of pregnancy, and eclampsia, the occurrence of convulsions (usually late in pregnancy) in a woman who fulfills the criteria for preeclampsia. Toxemia refers to the presence of pre-eclampsia or eclampsia.

Preeclampsia in otherwise healthy women is generally occurs during the first pregnancy, with an incidence of about 5%. Very young women and older women appear to be at increased risk. Blurred vision, although infrequent, is the most common symptom. Visual disturbances such as scotoma, diplopia, and dimness of vision, are seen in 30-50% of patients with eclampsia and 20-25% of patients with severe preeclampsia and hypertension. Photopsias may also be present in pre-eclampsia. Visual acuity changes may be significant, impending seizure in a preeclamptic patient, particularly in the post partum period. Though photic stimuli have been reported to predispose to seizures in susceptible patients, this risk is small compared to the benefit of the additional information provided by the ophthalmoscopic examination<sup>8,9</sup>.

The most common changes seen in toxemia are those of hypertensive retinopathy. The earliest and most common retinal change seen in toxemia is the development of focal (segmental) arteriolar spasm, which is reported in about 40 to 100% of preeclamptic patients, and is reversible in the majority of patients. Generalised arteriolar narrowing may also be seen frequently and resolves following pregnancy. Hemorrhages, exudates, diffuse retinal edema and papilloedema may also appear, but may be uncommon in patients without other systemic disease. Fetal mortality has also been correlated with severity of retinal changes, and a number of studies have recommended termination of pregnancy in the presence of severe retinopathy or rapidly progressing angiospastic changes. This is because retinal changes are thought to be a reflection of placental insufficiency on a vascular basis, and a premature infant would have a better chance of survival if it were delivered than if it remained compromised in utero. Also, a long duration of arteriolar changes and cotton wool spots may indicate the development of permanent maternal vascular and renal injury, and termination of pregnancy at the proper time might allow the systemic changes in the mother to regress. Conversely, the absence or regression of retinopathy has been used as a sign to allow a pregnancy to continue.

### Serous Exudative Retinal detachment

Serous exudative detachments have been reported to occur in 10% of patients with eclampsia and in 1-2% of patients with severe preeclampsia. They are usually bilateral and bullous, although cases with cyst-like

detachments have also been reported. The presence of a retinal detachment has not been reported to have an adverse effect on fetal prognosis. The detachment is thought to be due to choroidal vascular changes. Most patients with retinal detachments have full resolution of the detachment with return to normal visual function within a few weeks post partum. Occasional patients may have residual macular retinal pigment epithelial changes causing decreased visual acuity and some patients may also develop optic atrophy.

### **Visual Loss During pregnancy**

Transient cortical blindness has also been reported in eclampsia and occasionally in severe preeclampsia, in late pregnancy or shortly postpartum. Cerebral edema of the occipital lobes has been documented by CAT scan, with return to normal within a few weeks. Other causes of blindness or severely decreased vision during or immediately after pregnancy, with or without pre-existing toxemia, include retinal artery and vein occlusion, intracranial venous thrombosis, ischemic optic neuropathy and optic neuritis and psychogenic disturbance, in addition to retinal detachment, retinal edema, and changes in the occipital lobe as discussed above<sup>10</sup>.

### **Benign intracranial hypertension (Pseudotumour cerebri)**

Pseudotumour cerebri (PTC) is a clinical diagnosis, characterized by increased intracranial pressure, causing headache, papilloedema, and visual disturbances (including sixth cranial nerve palsy) without localizing neurological signs. It is more prevalent in women and is seen particularly in obese women of childbearing age. When it occurs in pregnancy, PTC usually appears in the first 20 weeks of gestation, although it may be seen in any trimester. Pregnant patients with the PTC appear to have the same rates of spontaneous abortion as the general population, and visual outcome for pregnant women with PTC is no different from that seen in non-pregnant women with this disorder.

Treatment of pseudotumour cerebri during pregnancy (i.e. bed, rest, lumbar punctures, subtemporal decompression, lumboperitoneal shunts or optic nerve sheath decompression) is the same as in any other patient with PTC, provided that the modalities used are not contraindicated due to risks to the fetus. However, the major exception is caloric restrictions (weight loss), which is prescribed because of the adverse effects of ketosis on the fetus. Visual acuity and visual fields must be monitored closely, with intervention as needed for threatened visual loss. While delivery or termination of pregnancy has been reported to cause amelioration of signs and symptoms, the availability of other modalities of treatment, e.g., corticosteroids, repeated lumbar punctures, and lumboperitoneal shunt, would suggest that termination of pregnancy is not indicated to treat PTC, except perhaps in very severe unresponsive cases. Carbonic anhydrase inhibitors are probably contraindicated in pregnancy<sup>11</sup>.

### **Coagulation disorders**

The possible coagulation disorders which may occur in pregnancy are disseminated intravascular coagulopathy (DIC), thrombotic thrombocytopenic purpura (TTP), and amniotic fluid embolism. DIC is a widespread process of thrombi formation in small vessels (choriocapillaries and adjacent arterioles and venules in the eye), which may occur in severe preeclampsia, abruptio placenta, and a retained dead fetus. Changes are generally limited to the submacular and peripapillary choroids. If the patient recovers from the systemic disorder, vision generally returns to normal with only mild pigmentary changes remaining.

Thrombotic Thrombocytopenic Purpura (TTP) is a rare disease which may be associated with pregnancy. Visual symptoms occur in about one tenth of cases, presumably due to serous sensory retinal detachment, arteriolar constriction, and disc edema. Retinal hemorrhages and exudates may also be seen. Other changes reported include anisocoria, subconjunctival hemorrhage, extraocular muscle abnormalities, and scintillating scotomas. Central nervous system involvement may occur causing homonymous hemianopia. Amniotic fluid embolism is a catastrophic event which occurs during labour/delivery shortly post partum, which has been reported to have been rarely associated with bilateral retinal arteriolar occlusions.

### **Effect on pre-existing conditions**

Normal pregnancy also influences various clinical conditions which may be present before conception (e.g. Diabetic retinopathy, intracranial tumours, high myopia, retinitis pigmentosa, Grave's disease, sarcoidosis, toxoplasmic retinochoroidopathy etc.).

### **Diabetic retinopathy**

The effect of pregnancy on a diabetic patient's eye depends to a great extent on the status of the patient's retinopathy at the start of pregnancy. A gestational diabetic (a previously non-diabetic woman, who becomes diabetic only during pregnancy) is not at risk for development of retinopathy. Diabetic women, who have no retinopathy before pregnancy, usually doesn't have any progression during pregnancy. For these patients, a single baseline ophthalmoscopic examination in the first trimester may be adequate unless visual

symptoms develop. It is worthwhile to repeat an examination in the third trimester to monitor for any changes in the retinal status. Patients with background diabetic retinopathy (BDR) at the start of pregnancy often follow a waxing and waning course during pregnancy. The retinopathy often worsens in the second trimester with clearing in the late third trimester and post partum. Patients with background retinopathy should probably be examined by an ophthalmologist at least once per trimester.

If a patient has no proliferative diabetic retinopathy at or before pregnancy, pre-proliferative changes, may appear during pregnancy. These patients develop soft exudates and blot hemorrhages which appear to be transitory changes of pregnancy and resolve in the postpartum period. Close observation of the patients who develop preproliferative change is probably warranted. In patients who develop proliferative diabetic retinopathy, aggressive scatter laser photocoagulation treatment of active neovascularization is warranted during pregnancy. This is especially true for patients with high risk characteristics i.e. neovascularisation of disc (NVD) of one fourth to one third disc area or more, neovascularisation of retina (NVE) of one third to half disc diameter or more with vitreous or preretinal hemorrhage, or NVD of less than one fourth disc area with preretinal or vitreous hemorrhage. When neovascularization is present without any of the three high risk characteristics, the clinical impression may often lead to practitioners to treat one or both eyes. A pregnant woman with active neovascularization may be at risk for vitreous hemorrhage during spontaneous delivery due to the valsalva action, which occur during the second stage of labour (Figure 3). Therefore, treatment of neovascularization and/or cesarean section may be considered in this type of situation. Proliferative retinopathy may regress at the end of the third trimester or postpartum without treatment. Proliferative diabetic retinopathy (PDR) by itself is no longer an indication for the termination of pregnancy or hypophysectomy to prevent blindness. This is in large measure due to the use of aggressive panretinal (PRP). If there is any indication for termination of pregnancy based on ocular considerations, the only one would be severe vision-threatening proliferative disease which is unresponsive to aggressive panretinal photocoagulation (PRP). For the patient with proliferative retinopathy, monthly ophthalmological evaluations would be indicated during pregnancy.

Earlier studies show a relationship between the severity of retinopathy in the mother and intrauterine death and congenital anomalies in the fetus, but the more recent studies have shown an improved prognosis for the fetus of a mother with diabetic retinopathy. The presence of BDR is generally not considered to place the pregnancy at any higher risk. It is now felt that, if a pregnant diabetic can be kept normoglycemic, the presence of retinopathy or nephropathy would not modify the course of the pregnancy, nor would the pregnancy adversely affect the retinopathy or nephropathy<sup>12</sup>.



**Figure 3:** Fundus and Fluorescein angiography picture of left eye of a pregnant woman showing proliferative diabetic retinopathy (PDR) with vitreous hemorrhage

### **Intracranial tumours**

The ability to induce ovulation by a variety of drugs (e.g. Bromocriptine) and thereby allow conception in women with amenorrhea or the amenorrhea galactorrhea syndrome has allowed many women with otherwise asymptomatic pituitary adenomas to become pregnant. A number of these women have developed the first signs and symptoms of a pituitary tumour (e.g., headache, visual disturbances, bitemporal visual field defects, decreased visual acuity, diplopia etc) during their pregnancies, with frequent resolution following delivery. Pregnancy may stimulate pituitary adenoma enlargement in the same way that a normal pituitary gland is affected, or it may cause increased growth of tumour. There are many reports in the literature of meningiomas, craniopharyngioma, lymphocytic hypophysitis presenting in pregnancy<sup>13</sup>.

### **High myopia**

There has been concern in the past regarding allowing high myopes to deliver spontaneously because of the changes in the pressure, induced by the valsalva mechanism in the second stage of labor. However, studies have now concluded that high myopes may be allowed to deliver spontaneously without deleterious effects on the eyes.

### **Retinitis pigmentosa (RP)**

A woman with retinitis pigmentosa (RP) may have visual field deterioration during pregnancy.

### **Graves disease**

Graves disease may be aggravated, or may present in early pregnancy. There may be some amelioration in the latter half of pregnancy, with recurrence in the postpartum period. Since normal pregnancy mimics in many ways the symptoms of thyrotoxicosis (e.g. tachycardia, diaphoresis, emotional liability, heat intolerance etc.), any eye findings, such as exophthalmos or lid lag may be helpful in making the diagnosis of thyrotoxicosis<sup>14</sup>. Treatment of Grave's disease should be managed by an experienced endocrinologist who can balance the benefits of various modalities with the risks to the fetus.

### **Ocular pharmacology in pregnancy**

One should be extremely cautious in administering any sort of medication to a pregnant woman, as in any other field of medicine. Fetal malformations have been reported with systemic use of atropine, homatropine and scopolamine. Systemic phenylephrine may cause club foot. So, topical instillation of these agents in the conjunctival sac for dilating the pupil is considered as a relative contraindication during pregnancy. However, if necessary, the measures to avoid systemic absorption of these agents from lacrimal passages and nasal mucosa should be employed as follows:

- Ask the patient to keep her eyes closed gently for 5 minutes maintaining pressure on the sac as suggested above.
- Instill only one drop in each eye at a time and wipe the excess medicine with tissue paper.

It should be emphasized that usually the benefits of a fundus examination outweighs the potential risks attributable to the mydriatic drops. Therefore, this cannot become a reason for not carrying out a fundus examination under mydriasis. Timolol is secreted and concentrated in breast milk in a woman taking this drug topically, so it should not be used in nursing mothers. Echothiophate iodide may cross through the placenta and may suppress the infant's pseudocholinesterase levels. Use of carbonic anhydrase inhibitors (e.g. acetazolamide) by pregnant mothers can cause cataracts in infants. Use of epinephrine can also produce similar kind (cataractogenic) of effects<sup>15</sup>. Pregnancy has a wide range of systemic effects on a woman and can have a potential impact on virtually any ocular condition. So, one should be very careful while performing any intervention or giving any drug to a pregnant woman, which may be harmful to the fetus.

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