

DIABETIC RETINOPATHY AND THE EFFECT OF PREGNANCY

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Conflict of interest: None

ABSTRACT

Pregnancy is associated with increased risk of development and progression of diabetic retinopathy (DR). Although pregnancy does not have any long term effect on DR, progression of retinopathy changes occur in 50%-70% of cases. The greatest risk of worsening occurs during the second trimester and persists as long as 12 months postpartum. The other factors found to be associated with its progression include duration of the diabetes, severity of retinopathy at conception, hyperglycaemic control, anaemia and progression of coexisting hypertension. Because of the increased risk of progression of the disease in pregnancy, conception should be delayed till the ocular disease is treated and stabilized and laser photocoagulation should be promptly instituted in all cases of severe non-proliferative retinopathy and should not be delayed till the patient develops early proliferative changes. Good diabetic control before and during pregnancy can help prevent this increase in the progression and serious vision loss.

Keywords: Diabetes mellitus, pregnancy, retinopathy, risk factors, laser photocoagulation.

Mallika PS, Tan AK, Aziz S, Asok T, Syed Alwi SAR, Intan G. Diabetic retinopathy and the effect of pregnancy. *Malaysian Family Physician*. 2010;5(1):2-5

INTRODUCTION

Pregnancy is a major risk factor for the progression of retinopathy and is definitely associated with increased prevalence and severity of retinopathy compared to non-pregnant diabetic women. Women with type I diabetes are particularly vulnerable to ocular changes during pregnancy. In the past prognosis for pregnancy in diabetic women with microvascular changes was so poor that many physicians advised either avoidance or termination of pregnancy, but currently due to the meticulous control of the blood sugar levels there has been a decrease in the incidence of foetal malformations. The risk factors for the progression of retinopathy in pregnancy are severity of retinopathy at conception, adequacy of treatment, duration of diabetes, metabolic control before pregnancy, and the presence of additional vascular damage (i.e. pre-existing or concomitant hypertensive disorder).¹ Pregnancy does not have a long term effect on the retinopathy. The retinopathy which progresses during pregnancy has a high tendency for regression in the

post-partum period.^{2,3} However, the length of time required for the regression is not exactly known.

The American Academy of Ophthalmology recommends that the pregnant diabetic women should have an ophthalmological examination before conception to determine the baseline severity and then again during the first trimester.⁴ Subsequent examination should be every 3 months until delivery.

Risk factors associated with progression of diabetic retinopathy (DR) during pregnancy

Duration of diabetes

Several studies have shown that younger the age of onset and longer the duration of the diabetes higher is the risk of progression of the disease. Progression of diabetic retinopathy (DR) was significant in those women with an early onset disease (14±8 years) than in women with a late onset disease (19±8 years).⁵ The risk of progression is again high if the duration of the diabetes is more than 15 years.⁶ Longer the

duration of the diabetes, higher is the chance for the development of microvascular complications, so these patients are likely to have a severe form of baseline retinopathy changes before pregnancy. Hence women with type I diabetes are encouraged to plan pregnancies early in life if possible.

Severity of retinopathy before pregnancy

Another important risk factor for the progression of DR during pregnancy is the degree of retinopathy prior to conception. Progression was more significant in women with moderate and severe forms of retinopathy compared to women with mild or no retinopathy at conception.⁶ In the Diabetes in Early Pregnancy Study (DIEP), 54.8% of women with moderate-to-severe non-proliferative retinopathy demonstrated disease progression whereas in women with mild retinopathy only 21.1% showed progression.⁷ Severe form of retinopathy changes is associated with poor perinatal outcome and in women with severe proliferative changes before conception, pregnancy has to be deferred till the disease is treated or stabilized.

Metabolic control

Poor metabolic control is definitely associated with disease progression not only in pregnant diabetic women but also in non-pregnant diabetic women. Patients with a higher level of glycosylated haemoglobin (7.5%) before conception are more likely to have progression of the disease. Intensive therapy during pregnancy to reduce the foetal and maternal complications has been found to increase the risk of progression of retinopathy. In the DIEP Study,⁷ it was clearly shown that those women with the greatest reduction in glycosylated haemoglobin during the first trimester were at an increased risk of progression of DR. DR is a microangiopathy and is associated with narrowing of the smaller calibre vessels. Intensive therapy results in decreased plasma volume which causes closure of the small retinal vessels that were narrowed but previously patent.⁸ In addition, sudden improvement in glycaemia control induces a decrease in the retinal blood flow, with resultant hypoxia and worsening of retinopathy.^{9,10} Intensive therapy is associated with a better perinatal outcome; but it may cause worsening of the retinopathy. So to have a better perinatal outcome without compromising visual loss due to DR, it is better to achieve a gradual good metabolic control before pregnancy rather than a rapid control during pregnancy.

Hypertension

Hypertension either pre-existing or pregnancy induced is a known risk factor for progression of retinopathy during pregnancy.¹¹ Pre-eclampsia was a potent risk factor for the deterioration of retinopathy in type I diabetic patients.¹² Increase systolic and diastolic pressure can affect the retinopathy.¹³

Pathophysiology of progression

The exact mechanism underlying the progression of retinopathy in pregnancy still remains unclear and several mechanisms have been suggested. Hormonal changes, changes in the systemic vasculature and retinal auto regulatory mechanisms may be responsible for the worsening of the retinopathy. Hormonal changes in pregnancy include increase plasma levels of human placental lactogen, oestrogen and progesterone hormones. Vascular changes induced by the elevated levels of oestrogen, progesterone and human placental lactogen may contribute to the progression of retinopathy in pregnancy. Of the 3 hormones, human placental lactogen (hPL) has a very important role in the effect of pregnancy on DR due to its enormous production and growth hormone-like activity. Pregnancy is associated with major changes in the systemic vasculature, which include augmentation in cardiac output and plasma volume and a decrease in the peripheral resistance.¹⁴ This results in a hyperdynamic circulatory state during pregnancy which potentially inflicts additional shear and stress and cause endothelial damage at the capillary level.¹⁵ The auto-regulatory mechanism is impaired in DR due to the loss of capillary pericytes and pregnancy may further worsen it. Thus in a diabetic patient, the physiological changes of pregnancy impose an added stress on an already compromised retinal circulation.

Effect of diabetic retinopathy on pregnancy

Several studies have addressed the issue of a possible relationship between the DR and the perinatal outcome. Women with severe form of disease are more likely to develop obstetric complications compared to women with no retinal or minimal retinal changes.¹⁶ Incidence of severe congenital malformations and/or foetal death is higher in patients with proliferative changes.¹⁷ The severity of retinopathy can be correlated with the presence of angiopathy elsewhere, especially the kidneys.^{18,19}

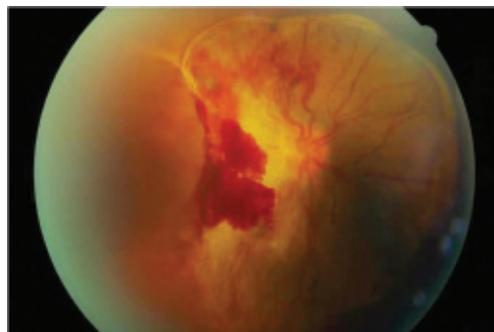


Figure 1: Colour fundus picture of right eye showing a total retinal detachment with pre-retinal haemorrhage and neovascularisation in a pregnant lady with severe proliferative diabetic retinopathy.

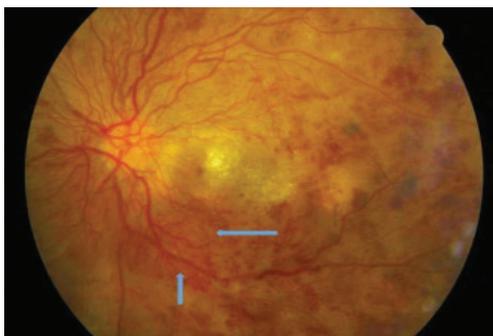


Figure 2: Colour fundus picture of the left eye showing extensive neovascularisation of the retina in the same patient.

Long term effect of pregnancy on diabetic retinopathy

Pregnancy does not cause any long term detrimental effects on the retina, kidney and peripheral nervous system.^{20,21} Retinopathy changes that have progressed during pregnancy have a tendency to regress after delivery. Even the severe proliferative changes show signs of regression in the post-partum period. As the progression of DR is attributed to the normal hormonal and physiological changes during pregnancy as well as improved glycemic control and high rates of hypertensive disorders, these changes regress after pregnancy.

Management of diabetic retinopathy during pregnancy

As DR can worsen during pregnancy, diabetic women should have a pre-conception counselling and follow-up by multi-disciplinary team consisting of endocrinologist, ophthalmologist and perinatologist. The patient should be clearly explained about the risk of progression of DR and the importance of

good metabolic control before and throughout pregnancy. Close follow-up is needed for patients with longer duration of pregnancy, severe baseline retinopathy, co-existing hypertension and renal disease.

Retinal assessment during pregnancy should be done by digital imaging with mydriasis using tropicamide following the first antenatal clinic appointment and again at 28 weeks if the first assessment is normal. If during the first assessment if there were any DR changes the patient should be seen again around 16-20 weeks. Women with preproliferative changes during pregnancy should have a 6 months follow-up after delivery. Vaginal delivery is not a contraindication in patients with DR.²²

A brief summary of recommendations¹³ for the management of diabetic patients planning pregnancy or already pregnant is given in Table 1.

In patients with longer duration of diabetes, every effort should be taken to achieve a good metabolic control preferably over a period of weeks or months before conception. If it is not possible, blood sugar levels should be normalized as soon as possible during pregnancy. A glycosylated haemoglobin level of more than 6 standard deviation above the control mean is associated with progression.⁷

Patients with severe non-proliferative and proliferative changes have a greater tendency for progression during pregnancy. So pregnancy should be deferred till the eye disease is treated and stabilized. If progression of the eye disease is noted during pregnancy, prompt laser photocoagulation is indicated in eyes with severe non-proliferative changes and should not be

Table 1: Recommendations for management of pregnant patients with type I DM to decrease the risk of progression of DR

Time period	Recommendations
Pre-conception	<ul style="list-style-type: none"> • Counsel diabetic women in childbearing years (especially those with pre-existing DR) about the risk of progression • Discuss postponement of conception until ocular disease is treated and stabilized • Diabetic patient should be brought under optimal glycaemia control before conception • Counsel patients about benefits of early pregnancy planning • Comprehensive eye examination to detect pre-existing DR and define the baseline level
First trimester	<ul style="list-style-type: none"> • Comprehensive eye assessment • Frequent monitoring of blood pressure • Tight glycemic control: First diet control and if blood sugar not controlled initiate insulin therapy
Second trimester and Third trimester	<ul style="list-style-type: none"> • Comprehensive eye examination at the discretion of the examiner, but preferably every 3 months until delivery • Monitor blood pressure • Tight glycemic control
Postpartum	<ul style="list-style-type: none"> • Conflicting recommendations • Some sources suggest frequent ophthalmologic surveillance for first year postpartum

delayed till proliferative changes develop, because proliferative changes tends to progress despite photocoagulation in some eyes. Laser photocoagulation is the mainstay of treatment for DR with reasonable outcomes.²³ Indications for surgery during pregnancy include: tractional retinal detachment, nonclearing vitreous haemorrhage and neovascular glaucoma. Retinal surgery in pregnant women may be difficult, because of the potential problem of pregnant women to lie flat for a considerable period of time. Moreover presence of neovascular glaucoma with vitreous haemorrhage may be associated with a poor visual outcome.

DR with proliferative changes also shows a strong tendency towards regression after delivery. Patients with severe changes should be closely followed-up in the post-partum period till the diabetic retinal changes stabilize. This includes close retinal surveillance during the first year postpartum.

CONCLUSION

Pregnancy is a prominent risk factor for the progression of retinopathy. Though development of sight threatening retinopathy is rare during pregnancy, it can have serious consequences for the mother and the foetus. Proper planning of pregnancy in young diabetic women and prompt laser photocoagulation of severe non-proliferative retinopathy can prevent serious sight threatening retinopathy. DR has a definite tendency for regression in the post-natal period and if the retinopathy is stable after delivery there is no risk of progression with subsequent pregnancies.

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