

# OCULAR COMPLICATIONS OF DIABETES MELLITUS IN PREGNANCY – CASE REPORT

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## SUMMARY

Pregnancy is associated with increased risk of progression of diabetic retinopathy (DR), the greatest risk of worsening occurs during the second trimester of pregnancy and persists as long as one year after the childbirth. The risk factors include duration of the diabetes, insufficient metabolic control, severity of DR at the time of conception and presence of coexisting vascular disease, such as arterial hypertension, and pregnancy itself. The recommendations for retinopathy screening in pregnancy vary significantly. A dilated fundus exam should be done in the beginning of pregnancy, the next follow-up throughout pregnancy depends on the severity of ocular findings. The cooperation of multi-disciplinary team consisting of ophthalmologist, obstetrician and endocrinologist is essential to provide the best health care.

The authors present a case report of a pregnant woman with type 1 diabetes mellitus (DM), who had a progression of DR and diabetic macular edema (DME) in both eyes during pregnancy. She has had DM for 24 years and has been treated with insulin. The patient was examined at the 23rd week of the second pregnancy (first pregnancy was terminated because of missed miscarriage). The diagnosis of advanced proliferative DR and advanced DME in both eyes was made so we performed panretinal laser photocoagulation of the retina of both eyes. Despite that the ocular findings got worse and we found vitreous haemorrhage in the left eye. We performed pars plana vitrectomy (PPV) of the left eye at the 28th week of pregnancy, nevertheless the DME got worse in both eyes, so we recommended to terminate the pregnancy at the 31st week because of the risk of loss of vision. The visual acuity of the left eye improved, but suddenly there was vitreous haemorrhage in the right eye after the delivery. We indicated PPV of the right eye, the outcome of the surgery was satisfying. We still take care about this patient.

**Key words:** diabetic retinopathy, diabetic macular edema, pregnancy, vitreous haemorrhage, vitrectomy, laser coagulation

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## INTRODUCTION

Pregnancy is associated with a higher risk of progression of diabetic changes on the ocular fundus, in which the greatest risk is in the second trimester of pregnancy and persists for several months to a year after childbirth [1]. In gestational diabetes there is zero risk of ocular complications [2]. The risk factors of progression of diabetic retinopathy (DR) during pregnancy include the length of duration of the disease, insufficient metabolic control of diabetes mellitus (DM), severity of DR before conception and the presence of other vascular pathologies, in particular arterial hypertension and preeclampsia, as well as the pregnancy itself [1,3-6]. The most important risk factor has been shown to be the severity of DR [5,7], which also correlates with the risk of congenital malformation of the foetus [3]. The recommendations for screening of diabetic changes

in pregnancy differ; of fundamental importance is examination of the ocular fundus in artificial mydriasis at the beginning of pregnancy, after which it is appropriate to adjust the intervals of follow-up examinations according to the severity of the finding, in which the maximum interval should be 3 months even in the case of an absence or minimum of diabetic changes on the ocular fundus [3]. We must also not neglect follow-up examinations of the ocular fundus during the first year of the post-natal period, even though there is a large chance of correction of diabetic changes after the end of pregnancy [5,6]. In order to attain the best quality care for pregnant diabetic patients, it is very important to ensure inter-disciplinary co-operation of an ophthalmologist, gynaecologist and diabetologist.

The authors present a case report of a pregnant patient on whom it was necessary to perform surgery for ocular complications of DM, due to the risk of loss of visual acuity (VA).

## CASE REPORT

A 36 year old female patient with type 1 diabetes reported to the general outpatient clinic of the Department of Ophthalmology at the University Hospital in Olomouc (FNOL), for an examination of the ocular fundus in order to exclude diabetic changes. She had been referred by the Department of Gynaecology and Obstetrics at FNOL, to where she had been transferred from the district hospital. The patient had undergone in vitro fertilisation (IVF), and in the 6th week of pregnancy had been admitted at a higher centre due to suspected silent miscarriage and progressing extraocular complications of DM.

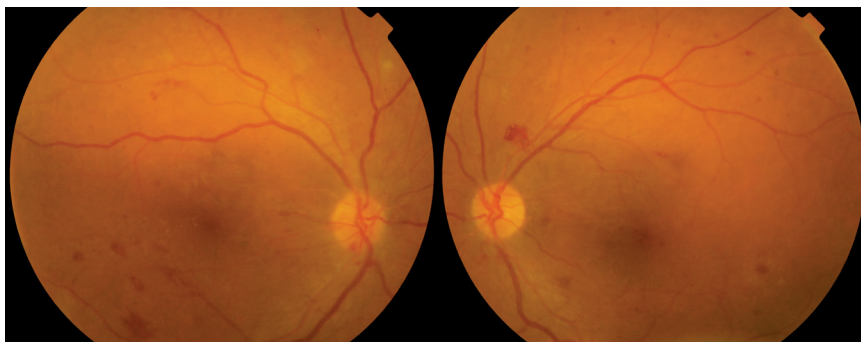
The patient had been treated for DM for a period of 24 years in intensified insulin regimen. She now had newly diagnosed arterial hypertension, and did not state any other general pathologies. Blood pressure was around the value of 150/85 mmHg, according to the documentation of her attending gynaecologist she had long-term decompensated DM with values of glycated haemoglobin within the range of 80-100 mmol/mol. She had hitherto been observed by the district ophthalmologist, and as regards her ophthalmological anamnesis, she wore glasses for distance vision and had not undergone any ocular surgery or suffered any ocular traumas.

At the first examination, VA was 6/9 bilaterally with correction, subjectively the patient did not perceive worsened vision. The anterior segment of both eyes was pacific, diffuse intraretinal haemorrhages and microaneurysms were present on the ocular fundus, and in addition in the left eye superficial neovascularisations above the papilla with preretinal haemorrhage (Fig. 1). Optical coherence tomography (OCT) of both eyes demonstrated minimal changes of the neuroepithelium, without diabetic macular edema (DME, Fig. 2). Due to advanced

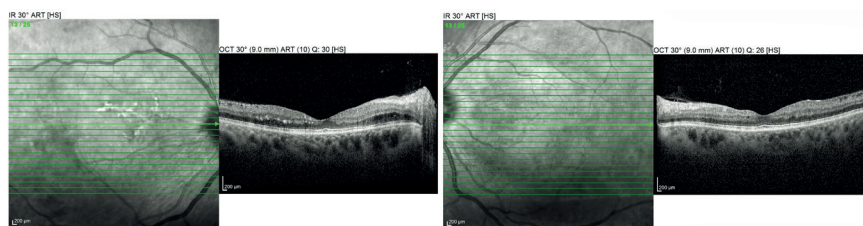
non-proliferative DR in the right eye and proliferative DR in the left eye we performed scatter laser photocoagulation (LPC) of the retina in the right eye and panretinal photocoagulation (PRP) of the retina in the left eye. The diagnosis of silent miscarriage was unfortunately subsequently confirmed, and the pregnancy was terminated. The patient did not report for a further planned follow-up, and was observed at the local ophthalmology outpatient clinic.

Nine months later the patient again underwent IVF, and in the 23<sup>rd</sup> week of her second pregnancy she was sent for an eye examination at the Department of Ophthalmology at FNOL, this time due to deterioration of VA. At the examination VA in the right eye was 40 letters of Early Treatment Diabetic Retinopathy Study (ETDRS) optotype, in the left eye 35 letters of ETDRS optotype. Objectively the anterior segments were pacific, irises without rubeosis, we recorded only incipient cortical opacity of the lenses. On the fundus of both eyes we observed advanced diabetic changes, in which in addition to haemorrhages, microaneurysms and numerous hard exudates there were also evident signs of ischemia, thus neovascularisation and papilloedema. There was present bilateral DME (Fig. 3), which according to OCT reached central retinal thickness (CRT) of 949  $\mu$ m in the right eye and 1505  $\mu$ m in the left eye (Fig. 4). We supplemented full PRP of the retina of both eyes, despite which the finding progressed further, and in the 28th week of pregnancy there was a deterioration of VA to 10 letters of ETDRS optotype in the left eye, where partial haemophthalmos newly appeared; VA in the right eye was maintained on the level of 48 letters of ETDRS optotype.

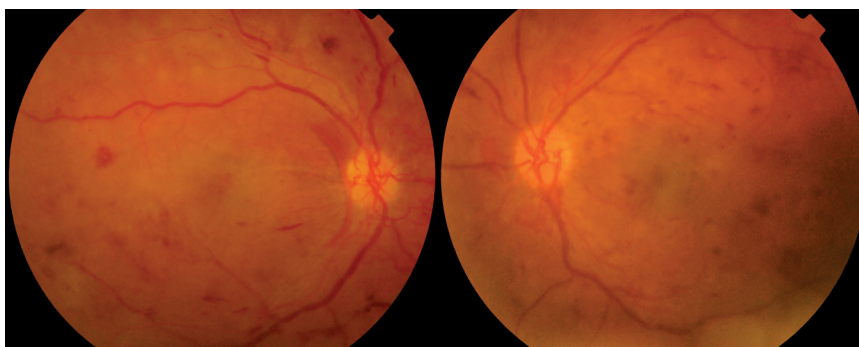
Even despite this finding, the gynaecologists refused to terminate pregnancy by caesarean section prematurely due to the immaturity of the foetus, and as a re-



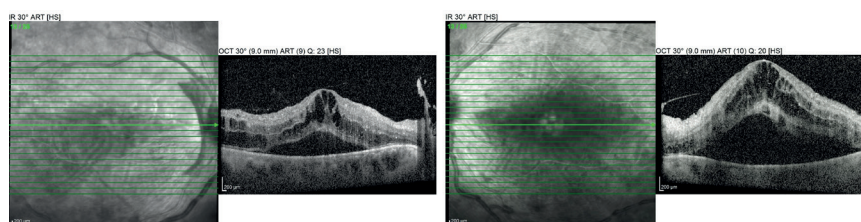
**Fig. 1.** Photograph of ocular fundus of both eyes in 6th week of first pregnancy



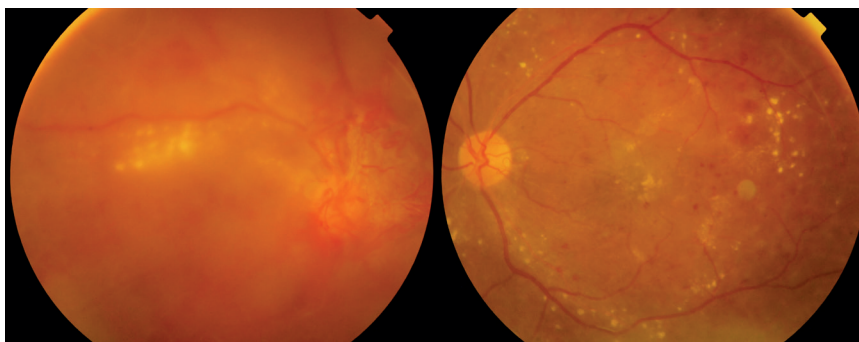
**Fig. 2.** OCT examination of both eyes in 6th week of first pregnancy



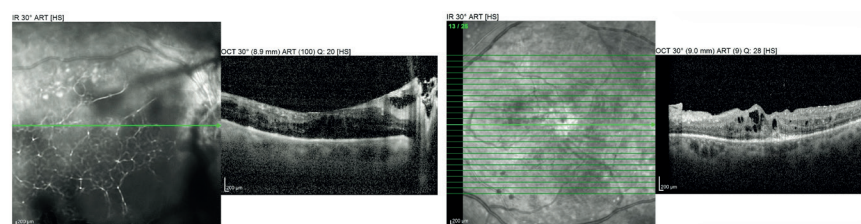
**Fig. 3.** Photograph of ocular fundus of both eyes in 23rd week of second pregnancy



**Fig. 4.** OCT examination of both eyes in 23rd week of second pregnancy



**Fig. 5.** Photograph of ocular fundus of both eyes 3 months after childbirth



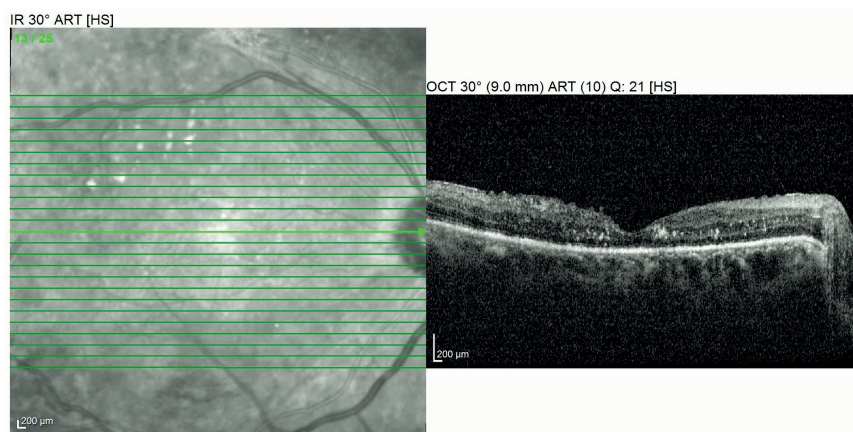
**Fig. 6.** OCT examination of both eyes 3 months after childbirth

sult it appeared most suitable to proceed to a surgical solution of the diabetic complications in the left eye by means of pars plana vitrectomy (PPV) with internal air tamponade and treatment of the periphery of the retina by cryocoagulation, which we performed in the 28th week of pregnancy under local anaesthesia. Despite her advanced pregnancy, the patient co-operated well and the procedure took place without complications. At a follow-up examination two weeks after PPV, the post-operative finding in the left eye was with dispersion of blood in the vitreous body, referential performance of OCT examination did not demonstrate significant re-

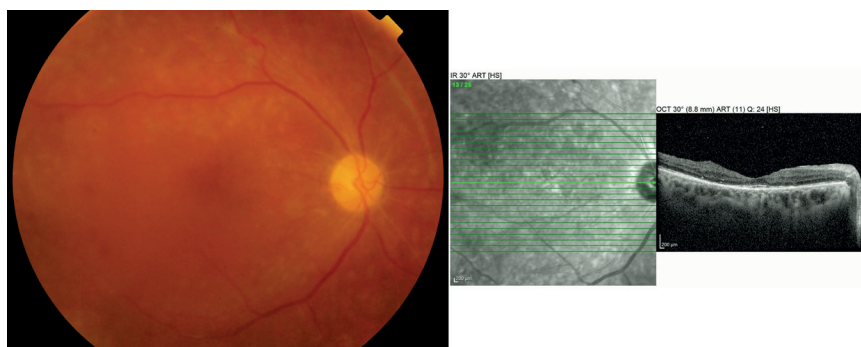
gression of DME, CRT reached the value of 1325  $\mu\text{m}$ . In the right eye also the finding had not improved, CRT remained on the level of 873  $\mu\text{m}$ , and VA in this eye had deteriorated to 35 letters of ETDRS optotype. In the 31st week, upon our recommendation the gynaecologist indicated the patient for planned termination of the pregnancy due to the risk of permanent damage to the mother's sight. The pregnancy was terminated by means of caesarean section without complications, and the child was perfectly healthy.

Three months after childbirth the finding in the left eye progressively regressed (Fig. 5), after absorption of the





**Fig. 7.** OCT examination of right eye 2 months after surgery (5 months after childbirth)



**Fig. 8.** Photograph of ocular fundus and OCT examination of right eye 11 months after surgery

internal tamponade VA improved from 10 to 35 letters of ETDRS optotype and CRT was reduced to 401 µm (Fig. 6). However, partial haemophthalmos developed in the right eye (Fig. 5), with a further deterioration of VA to 15 letters of ETDRS optotype, CRT 420 µm (Fig. 6). We therefore performed PPV on the right eye under local anaesthesia with air endotamponade. Two months after surgery there was a rapid reduction of CRT from 873 µm to 182 µm (Fig. 7), and VA improved to 50 letters of ETDRS optotype.

The patient did not return for a further follow-up examination for a further eight months, when she complained of deteriorated vision in the left eye. The finding was satisfactory almost one year after surgery, VA 55 letters of ETDRS optotype, macula without edema, fundus without active neovascularisations (Fig. 8), but in the left eye there was recurrence of haemophthalmos with a deterioration of VA to the level of movement in front of the eye. We again indicated PPV, but the patient deferred the operation due to extraocular complications of DM. We remain in contact with the patient, according to her words haemorrhage into the vitreous body has been absorbed, we do not yet have the current ocular finding available.

## DISCUSSION

DR is the most common ocular pathology, which may progress during the period of pregnancy. The mechanisms by which the progression of DR is caused by preg-

nancy itself are not precisely known, but hormonal and haemodynamic changes are presumed [4]. In as many as 50 % of cases pregnancy may worsen existing advanced form of DR, although transition to proliferative form is rather an exception [2]. Already present DME may also worsen during the course of pregnancy, and it is therefore appropriate to perform fluorescence angiography (Fag) on patients with incipient DME, even before the start of pregnancy in the case of planned IVF. We do not perform Fag during pregnancy or breastfeeding, although no teratogenic or mutagenic effect of fluorescence has yet been demonstrated [2].

For patients with DM, pregnancy should always be planned, and should take place during a time of stabilisation of the pathology. Women of fertile age should have a level of glycated haemoglobin up to 70 mmol/mol, and maintain it for at least 6-8 months before conceiving [3]. Rapid compensation of DM at the beginning or during the course of pregnancy may be accompanied by a higher risk of occurrence of DME, which is generally known in all patients treated for DM [2,3,8]. It is necessary to perform regular examinations of the ocular fundus in artificial mydriasis, which the patient should undergo at the beginning of pregnancy; afterwards it is suitable to adjust the intervals of examinations according to the severity of the finding, in which the maximum interval should be 3 months even in the case of an absence or minimum of diabetic changes on the ocular fundus [3]. We must also

not neglect follow-up examinations of the ocular fundus during the first year of the post-natal period.

The standard treatment of DR also in pregnancy remains LPC of the retina, which does not represent any risk to the foetus [2]. PRP should be performed already in the stage of advanced non-proliferative DR, because proliferative changes may progress despite sufficient laser treatment [4]. In the case of progression of the finding and the onset of complications of DR (non-resorbing haemophthalmos, tractional retinal detachment, neovascular glaucoma), even despite sufficient laser treatment in some cases it is necessary to proceed to surgical intervention [1].

Other than good control of DM, the gold standard in the treatment of DME in pregnancy is considered to be LPC of the macula [9]. In the case of DME which is resistant to laser treatment, a safe alternative is intravitreally applied corticosteroids [9]. However, we must always take into consideration the local adverse effects of this treatment, since corticosteroids may lead to the development of cataract and steroid glaucoma. At present treatment using preparations blocking vascular endothelial growth factor (anti-VEGF) is preferred in the treatment of DME: Ranibizumab (Lucentis; Novartis Pharma AG, Basel, Switzerland) and Aflibercept (Eylea; Bayer HealthCare, Berlin, Germany). According to the FDA (Food and Drug Administration) classification of medications for use in pregnancy, these are classified in category C, which means that there are no controlled trials on pregnant women, no trials on animals which would demonstrate any adverse effects on the foetus, or that no scientific data is available [10]. As a result, this therapy is not recommended during the course of preg-

nancy due to the potential risks for the foetus [3].

In complicated cases, surgical therapy of DR and DME is an alternative which may be performed also during pregnancy, as we have presented in our case report. However, the procedure should always be performed by an experienced vitreoretinal surgeon, since this mostly concerns advanced findings. Furthermore, it is essential to ensure good co-operation from the pregnant patient, for whom the position of lying on her back throughout the period of the operation may be demanding.

DR is not a contradiction for spontaneous childbirth, but it is necessary to exercise caution in the case of proliferative form of DR, in addition with recurring haemophthalmos [8]. In order to attain the best quality care for pregnant diabetic patients, it is very important to ensure inter-disciplinary co-operation of an ophthalmologist, gynaecologist and diabetologist.

## CONCLUSION

As illustrated by the presented case report, pregnancy is a significant risk factor in the progression of DR. It is of fundamental importance to plan pregnancy during a time of long-term compensation of glycaemia and stabilisation of the ocular finding. We must place emphasis also on the education of all patients with DM in fertile age, in whom regular examinations of the ocular fundus are a standard requirement. Although sight-threatening DR is rare, it may have very serious consequences, and as a result it is of fundamental importance to select such a procedure which will not lead to damage to the mother's sight while at the same time enabling sufficient development of the foetus.

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