Retinal Outcomes in Proliferative Diabetic Retinopathy Presenting during and after Pregnancy

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Background: The aim of this study was to determine retinal outcomes in patients with proliferative diabetic retinopathy (PDR) presenting during pregnancy or within the first year postpartum.

Methods: All patients with diabetes mellitus during pregnancy from 1992 through 2002 were included. Medical records were reviewed and data including obstetric history, pregnancy outcome, other medical complications, and course and management of retinal disease were analyzed.

Results: The study group comprised 6 women with a total of 7 pregnancies complicated by PDR during pregnancy or during the first year postpartum. Two of these pregnancies were in patients who had long-standing PDR and had received panretinal photocoagulation prior to pregnancy. Both of them had stable retinas during pregnancy and during the postpartum period. Three patients (4 eyes) who presented with high risk PDR during pregnancy required either repeated laser therapy (3 eyes) or vitrectomy (one eye) during the first year postpartum. Two patients (3 eyes) who did not have PDR at delivery developed PDR during the first year postpartum. After the second year postpartum, nine eyes which had developed PDR during or post pregnancy had stable retinas, two had developed phthisis, and one manifested end stage PDR.

Conclusions: Because of the persistent adverse effects of pregnancy on the retinas of women with diabetes mellitus, meticulous retinal surveillance and appropriate therapy are important not only during pregnancy but also during the postnatal period.

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Key words: **pregnancy, diabetic retinopathy, proliferative retinopathy, proliferative diabetic retinopathy.**

Retinopathy affects 20 to 27% of women with diabetes mellitus in the reproductive-age group.[1,2] Pregnancy is a prominent risk factor for the development and progression of retinopathy in women with insulin-dependent diabetes mellitus (IDDM).[2-5] Reported rates of progression of retinopathy ranged from 17% to 70%.[4,6-10] The mechanisms by which pregnancy might alter the course of retinopathy are not entirely clear. The adverse effects of pregnancy on retinal status persist into the first year postpartum.[3-5] The baseline level of retinopathy at conception is a major risk factor for progression of

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retinopathy.[11-13] Proliferative diabetic retinopathy (PDR) manifests with ischemia and neovascularization, which can cause vitreous hemorrhage and retinal detachment resulting in rapid visual deterioration. In the past, PDR was even considered a relative contraindication to pregnancy. Termination of pregnancy to avoid permanent visual loss in patients with proliferative retinopathy had been advocated.[14,15] In this report, we describe the retinal outcomes of women with PDR presenting either during pregnancy or during the first year postpartum.

METHODS

From 1992 through 2002, all patients at our hospital with the diagnosis of diabetes mellitus during pregnancy were included in the study. Medical records were reviewed and data including obstetric history, pregnancy outcome, other medical complications, and course and management of retinal disease were collected.

Ophthalmic management included dilated fundus examination, fundus photography, fluorescein angiography (either before or after pregnancy), panretinal photocoagulation (PRP) for patients with high risk PDR, and vitreoretinal surgery. Retinopathy grade was classified according to the criteria of the Wisconsin Epidemiological Study on Diabetic Retinopathy as follows: (1) No retinopathy. (2) a. Less than 20 hemorrhages and /or microaneurysms, or b. Cotton wool spots alone. (3) a. More than or = 20 hemorrhages and /or microaneurysms, or b. Hard exudates combined with any number of hemorrhages and /or microaneurysms, or c. Less than 5 cotton wool spots combined with hemorrhages and /or microaneurysms or hard exudates. (4) More than or = 5 cotton wool spots or intraretinal microvascular abnormalities (IRMA) of vessels combined with hemorrhages and /or microaneurysms with or without hard exudates. (5) Venous bleeding combined with hemorrhages and /or microaneurysms with or without hard exudates, IRMA vessels or cotton wool spots. (6) Proliferative retinopathy, or scars of photocoagulation known to have been directed at new vessels.[16]

RESULTS

A total of 73 women diagnosed with of insulin-dependent diabetes mellitus (IDDM) during pregnancy during the ten-year study period were included. Six women (8.2%) had a total of seven pregnancies complicated by PDR during pregnancy or during the first year postpartum. Case summaries for these six patients are shown in Table 1. The mean maternal age was 30 years and mean duration of diabetes was 9 years. Two women had diabetes for more than 10 years at the time of pregnancy. Two women had history of abortion. Of the 2 women with the pregnancy complicated by preeclampsia, one decided to terminate the pregnancy at gestation week 16 and the other delivered a premature infant at week 29. Six continuing pregnancies resulted in live births at a mean gestational age at delivery of 35 weeks with a

Table 1. Clinical Summary of 6 Patients with Pregnancy

Patient No.	Age	Duration of diabetes (year)	Obstetric history	Mode of insulin use	Delivery mode	Pregnancy complication	Gestation age of delivery (weeks)	Birth body weight (gm)
1	28	13	G1P0	C	C/S	None	38	3500
	32	17	G2P1	C	C/S	None	34	3110
2	28	5	G1P0	C	Termination in early pregnancy	Preeclampsia, nephropathy	abortion in gestation week 16	-
3	37	7	G4P0A3	C	C/S	Preeclampsia	29	884
4	32	12	G1P0	C	C/S	None	34	2200
5	25	0†	G1P0	C	C/S	None	40	3101
6	31	8	G3P0A2	C	C/S	None	35	3660

Abbreviations: P: pregnancy; GxPyAz: times of gestation, partum, and abortion; C: conventional; C/S: cesarean section.

mean birth weight of 2743 gm. Gestational age was over 36 weeks at the time of 2 of the 6 deliveries. Two of 6 live births had birth body weights below 2500 gm, respectively. Among the 5 deliveries by cesarean section in 5 women; one was a repeat cesarean section and 4 were primary.

The ophthalmic data (6 patients; 12 eyes) before, during, and after pregnancy is shown in Table 2. Two patients (4 eyes) with a total of 3 pregnancies had long-standing PDR and underwent PRP prior to pregnancy. Both of these patients had stable retinas and none required laser therapy either during gestation or during the postpartum period. Three patients (4 eyes) presented with high risk PDR during pregnancy and received PRP during gestation. Among the four affected eyes in these patients, one eye had stable retinal appearance and the other three required repeated laser therapy (3 eyes) or vitrectomy (one eye) during the first year postpartum. One patient presented with PDR and total retinal detachment of her left eye at the beginning of pregnancy. This patient asked to continue the pregnancy and did not receive any ophthalmic treatment to her left eye. She also had the complications of preeclampsia and nephropathy during pregnancy and terminated the pregnancy at gestation week 16. In the second year postpartum, the left eye of this patient showed phthisis and the fellow eye was in the end stage PDR. Two patients (3 eyes; patient No. 4 and 6) who had non-PDR after delivery developed high risk PDR during the first year postpartum (Table 2). After PRP, two of the affected eyes in these patients became stable and the other eye required vitrectomy because of vitreous hemorrhage. After multiple surgeries, this eye developed phthisis.

Table 2. Ophthalmic Data before, during, and after Pregnancy

Patient No.	Eye	Prepregnancy		Pregnancy		1st year Postpartum		2nd year Postpartum		Final retinal status*
		D	T	D	T	D	T	D	T	
1	R	PDR	PRP	RPDR	M	RPDR	M	RPDR	M	Stable
(1st P)	L	PDR	PRP	RPDR	M	RPDR	M	RPDR	M	Stable
	R	RPDR	M	RPDR	M	RPDR	M	RPDR	M	Stable
(2nd P)	L	RPDR	M	RPDR	M	RPDR	M	RPDR	M	Stable
2	R	Unknown	None	PDR	PRP	Progressive PDR	PRP	End stage PDR	M	End stage PDR
	L	Unknown	None	PDR with total TRD	None	PDR with total TRD	None	Phthisis	None	Phthisis
3	R	PDR	PRP	RPDR	M	RPDR	M	RPDR	M	Stable
	L	PDR	PRP	RPDR	M	RPDR	M	RPDR	M	Stable
4	R	Normal†	M	Unknown	None	Progressive NPDR‡	PRP	RPDR	M	Stable
	L	Normal†	M	Unknown	None	Progressive NPDR‡	PRP and VT	PDR with RD	VT and SB	Phthisis
5	R	Unknown	None	PDR	PRP	RPDR	M	RPDR	M	Stable
	L	Unknown	None	PDR	PRP	Progressive PDR	PRP	RPDR	M	Stable
6	R	Unknown	None	NPDR II	M	Progressive NPDR‡	PRP	RPDR	M	Stable
	L	Unknown	None	PDR	PRP	Progressive PDR	PRP and VT	RPDR	M	Stable

Abbreviations: D: diagnosis; T: therapy; P: pregnancy; PDR: proliferative diabetic retinopathy; PRP: panretinal photocoagulation; RPDR: regressed proliferative diabetic retinopathy; M: monitoring; TRD: tractional retinal detachment; NPDR: nonproliferative diabetic retinopathy; VT: citrectomy; SB: scleral buckling.

* Final retinal status over 2 years postpartum

† Retinal status 2 years before pregnancy

‡ Progression of retinopathy from grade 5 to 6

II Diabetic retinopathy grade 5

DISCUSSION

The baseline level of retinopathy at conception is the major risk factor for progression of diabetic retinopathy.[11-13] The results of the Diabetes in Early Pregnancy Study (DIEP) demonstrated that women with mild or more severe retinopathy at the time of conception were at high risk for progression of retinopathy during pregnancy. The progression rates from nonproliferative retinopathy to proliferative retinopathy in the DIEP study were 6.76% and 30% in patients whose baseline retinopathies were mild and moderate, respectively.[11] PDR represents an advanced state of microvascular disease found in long-standing diabetes patients, which can cause vitreous hemorrhage and retinal detachment resulting in rapid deterioration of the vision. Development or deterioration of PDR during pregnancy is uncommon and has been reported to occur in 2% to 11% of pregnancies in diabetics.[4,11,17] However, few researchers have assessed the outcomes in pregnant or postpartum patients with this severe retinal disease.[17-20] It remains unclear whether the counseling patients often received, which discourages conception or the continuation of pregnancy in the presence of PDR, is justifiable. In fact, it is unethical and impossible to answer this question with a randomized, prospective study. Hence, studies of related questions will have to be used in a retrospective design. The patient with the most severe complications in this study (patient 2) developed PDR and total retinal detachment in her left eye at the beginning of pregnancy. Whether to terminate the pregnancy immediately in order to slow the progression and allow for further ocular surgery or to continue the pregnancy in accordance with the strong desires of the mother was a complex problem. After considering the options, the patient asked to continue the pregnancy and did not receive any treatment to her left eye. Unfortunately, phthisis developed in the left eye and the fellow eye had end-stage PDR during the second year postpartum.

Several important risk factors can contribute to the aggravation of diabetic retinopathy, including the pregnancy itself,[4,8] duration of the diabetes,[17,21,22] elevated glycohemoglobin level,[8,17,22] rapid normalization of blood glucose level,[5,23,24] hypertension,[25] renal disease,[4,6,9,20,26] and the degree of retinopathy at the beginning of pregnancy.[6,8-10] The adverse effects of pregnancy on retinal status can persist into the first year postpartum.[3-5] In one report about retinal outcomes in the presence of PDR, laser therapy was required during 60 % of pregnancies, and in 65 % of pregnancies, treatment was also needed during the postpartum period.[18] In our study, three patients (4 eyes) presented with high risk PDR during pregnancy and all received PRP during gestation. Three of these eyes required repeated laser therapy or vitrectomy (one eye) during the first year postpartum.

Progression of PDR may depend on whether laser photocoagulation has been performed before pregnancy. Treatment of PDR with laser before pregnancy may lessen the progression during pregnancy.[17,18,27] In one review of 81 patients who had not been treated before pregnancy, 47 (58%) progressed. In contrast, of 35 patients who had received any laser photocoagulation before pregnancy, only 9 (26%) progressed.[27] In our study, two patients (4 eyes) with a total of three pregnancies had undergone PRP prior to pregnancy. None of them required laser therapy either during pregnancy or during the postpartum period. Therefore, it is important that proliferative retinopathy is detected and treated, preferably before the onset of pregnancy. Three patients in our study did not have any clinical records of retinal status before pregnancy. This finding suggests that women with diabetes mellitus in the reproductive-age group need better patient education about the how to establish good glucose control and the need to thoroughly monitor retinal status.

Data on the long-term effects of pregnancy on diabetic retinopathy are controversial. Some researchers reported that retinal status in diabetics with multiple pregnancies was better in comparison with women matched for age and duration of diabetes.[28,29] Complete or partial regression of retinopathy after delivery has been reported.[6,22,29] The effects of pregnancy on retinal status are considered to be relatively transient; most changes revert to pre-pregnancy levels within a year or more after the end of pregnancy.[4] However, the adverse effects of pregnancy on retinal status persists into the first year postpartum.[3-5] Pregnancy motivates diabetic women to achieve better metabolic control but it is not known if this motivation persists postpartum or if motherhood worsens the situation due to nursing the newborn child and lack of time for self care. In our study, 2 patients (3 eyes) presented with non-PDR after delivery but developed high risk PDR during

the first year postpartum. After management, two eyes became stable but the other one developed phthisis. Thus, increased retinal surveillance by a retinal specialist should continue during the first year postpartum.

In conclusion, women with diabetes mellitus who are in the reproductive-age group are especially in need of education about adequate glucose control and ophthalmic surveillance. In addition, patient education should explain the need for laser photocoagulation to be performed before pregnancy in women who have PDR and plan to become pregnant, in order to avoid progression of retinopathy during pregnancy. Because of the persistent adverse effects of pregnancy on the retina, meticulous retinal surveillance and appropriate therapy are important not only during pregnancy but also during the postnatal period.

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在懷孕中及生產後發生增生性糖尿病網膜病變之預後

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背 景： 研究在懷孕中及生產後1年內，發生增生性糖尿病網膜病變婦女的網膜預後。

方 法： 自1992年至2002年，回顧分析所有診斷爲糖尿病且懷孕的病例。記錄其產科的病史、生產的結果、內科的併發症、網膜疾病的病程與處理。

結 果： 總共6位女性 (8.2%) 於7次懷孕當中，在懷孕中及生產後1年內發生增生性糖尿病網膜病變。其中2位在共3次的懷孕中，因先前的增生性糖尿病網膜病變已經接受全網膜雷射凝固術治療，這2位女性的網膜，在懷孕中及生產後都很穩定。3位女性 (其中4眼) 在懷孕中表現出高危險性之增生性糖尿病網膜病，其中3隻眼在產後1年內，需再接受雷射凝固術治療或玻璃體切除手術 (其中1眼)。2位女性 (其中3眼) 在生產後表現出非增生性糖尿病網膜病變，但是於產後1年內惡化至增生性糖尿病網膜病。於生產2年後，共9隻眼仍保持穩定的網膜，2隻眼演變至萎縮，1隻眼演變至末期增生性糖尿病網膜病變。

結 論： 因爲生產會導致糖尿病網膜病變的惡化，小心的網膜監視及適當的治療，不僅在懷孕中，而且在生產後都很重要。

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關鍵字： 懷孕，糖尿病網膜病變，增生性網膜病變，增生性糖尿病網膜病變。

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