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Effect of Pregnancy on Diabetic Retinopathy

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Objective: To establish the effect of pregnancy on progression of diabetic retinopathy and the correlation between diabetic retinopathy during pregnancy with age, glucose control and duration of diabetes.

Setting: Obstetric, Medical and Ophthalmology clinics.

Methods: This is a retrospective study of pregnant patients who attended obstetric, medical and ophthalmology clinics during January 1996 till December 1998. Non-pregnant diabetic patients in reproductive age groups who attended medical and ophthalmology clinics during the same period served as controls. A total of 60 pregnant insulin dependant patients were studied while 80 non-pregnant insulin dependant diabetics served as control.

Results: Diabetic retinopathy was found in 58% (35 patiens) of pregnant women, while it was present in 30% (24 patients) of the controls. Background diabetic retinopathy was found in 20 pregnant patients, in 3 of them (15%) progression to proliferative retinopathy occurred. Proliferative retinopathy was found in 15 patients. Two out of 7 patients (29%)of photocoagulation- treated group progressed to severe form while 5 out of 8 patients (62.5%)of the untreated group developed progression. Twenty-four of the 80 control patients (30%) had retinopathy. No progression occurred in the patients with no-retinopathy or in controls. Duration of diabetes was the only significant factor in progression of disease.

Conclusion: Understanding the risk factors contributing to aggravation of diabetic retinopathy during pregnancy is helpful in designing criteria for the team management of pregnant patients with diabetes. Pregnancy may deteriorate retinopathy and photocoagulation prior to pregnancy may protect against rapidly progressive proliferative retinopathy and visual impairment. Therefore, in diabetic women a full retinal evaluation must be done as a part of pre-pregnancy counseling procedure.

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The most common form of vascular diseases in diabetes is retinopathy .The overall prevalence of retinopathy in diabetes is 38%, and 85-90% of all diabetic patients have some manifestations of retinopathy after 25 years of diabetes mellitus[1,2]. Diabetic retinopathy affects 20-30% of diabetic women in reproductive age group[3]. The influence of pregnancy on the progression or amelioration of retinopathy has been controversial[4-7], but recent studies reported that pregnancy has an unfavorable influence on retinopathy[8-10].

Pedersen has demonstrated that there is an increased risk of vitreous hemorrhage and progression to blindness in patients who already have proliferative retinopathy[11]. There are several possible interdependent pathogenic mechanisms of diabetic retinopathy; breakdown of blood-retinal barrier has been mentioned, which could be due to retinal capillary occlusion, perhaps related to platelet adhesion and aggregation, or decreased fibrinolysis[12].

It was found that progesterone and human placental lactogen levels in pregnant patients with diabetic retinopathy are higher than those without. It is possible that placental hormones are one of the factors contributing to capillary occlusion and microinfarcts observed in the retina in many of patients with diabetic retinopathy[13]. Another mechanism is that progesterone may contribute to the worsening of diabetic retinopathy by upregulating intraocular vascular endothelial growth factor levels[14].

The aim of this study is to establish the effect of pregnancy on progression of diabetic retinopathy and the correlation between diabetic retinopathy during pregnancy with age, glucose control and duration of diabetes.

METHODS

A retrospective study of diabetic patients who attended the obstetric, medical and ophthalmology clinics from January1996 to December1998. The detailed records of 60 patients were available. Data were obtained for age, duration of diabetes mellitus, and control of diabetes as measured by fasting blood glucose. Records of non-pregnant insulin dependant diabetic patients in the reproductive age who attended the medical and ophthalmology clinics served as controls; a total of 80 patients' data were randomly recorded.

Results of detailed ophthalmologic examination and whether the patients had received photocoagulation prior to or during pregnancy were recorded for both groups.

The values for plasma glucose before and during pregnancy were obtained by taking a mean of all fasting venous plasma glucose values obtained from a particular patient in 6 months preceding pregnancy and during 9 months gestation and mean fasting blood sugar for the control group for the same period (15months).

The patients were classified into 3 groups according to the ophthalmological findings:

Group 1: No retinopathy
Group 2: Background retinopathy (BGDR)
* Mild BGDR <50 microaneurysms
* Moderate>50 microaneurysms, soft and hard exudates
*Extensive BGDR-cotton wool spots, waxy exudates, and vitreous hemorrhage
Group 3: Proliferative retinopathy (PDR)
*Mild PDR- new vessel elsewhere
* Severe PDR- new vessels on or within one disc diameter of the optic disc and possibly elsewhere

Progression or regression of diabetic retinopathy (DR) was defined as meeting the clinical characteristics of a group or subgroup to which the patient was not initially assigned.

RESULTS

Of the 60 pregnant patients with insulin dependant diabetes (IDDM), 35 patients (58%) were found to have diabetic retinopathy at first examination while it was present in 24 patients (30%) of control group.

None of the 25 patients who were not affected by retinopathy at first examination developed retinopathy during pregnancy (group1).

Background retinopathy was found in 20 patients (group 2), one of them having an extensive form of background diabetic retinopathy which progressed to severe proliferative retinopathy. Another 2 patients were having moderate BGDR and in these progression to mild proliferative retinopathy occurred, making a total of 3 patients with progression of the disease (15%). In all of these three patients, arrest of progression was achieved by photocoagulation, which was done after delivery.

Untreated mild proliferative retinopathy was found in 8 pregnant patients at initial examination, 5 of them experienced progression from mild to severe PDR during pregnancy (62.5%). All of these patients received photocoagulation during pregnancy, which resulted in stabilization of the retinal disease.

Seven of 35 patients who were found to have mild PDR were treated by photocoagulation prior to pregnancy. In this group, only 2 patients (29%) experienced progression of their retinal disease to severe form which required additional photocoagulation during pregnancy.

Of the 80 non-pregnant insulin dependant diabetic patients in the reproductive age group, 24 patients (30%) had retinopathy which did not progress during 9 months period.

These results are summarized in the table1 and fig.1 shown below:

Table 1. **Retinopathy progression in the reproductive age group of non-pregnant insulin dependant diabetic patients**

Patients	Control	Group 1	Group 2	Group 3	
Retinopathy (Number)	24	0	20	15 Untreated	Treated 7
Progression of Retinopathy (%)	0%	0%	15% (3)	62.5%(5)	29%(2)

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Figure 1. Progression of Retinopathy in different age groups

The relationship between the age, glucose control and duration of diabetes are shown in the following Table2

Table 2. **Relationship between age, glucose control and duration of diabetes mellitus**

Group	Number	Mean age	Serum glucose (mean) (mmol/l)	Duration of Diabetes Mellitus (years)
Group one	25	26.5	2.7	6.0
Group two	20			
a. No progression	17	28	2.8	10.7
b. Progression	3	27.3	3.4	15.7
Group three	15			
a. No progression	8	30	3.2	9.5
b. Progression	7	27.8	3.2	14.6
Control	80	27	2.9	11.5

From these results we conclude that the duration of diabetes is a significant factor for the development of DR (p value<0.005), while no significant effect of mean age and controllability of diabetes mellitus on it (p value >0.05). Duration was also important for the progression of the disease; it was longer for those whose retinopathy progressed during pregnancy in both groups 2 and 3(15.7 vs. 14.6).

DISCUSSION

Diabetic retinopathy is the leading cause of blindness between the age of 24-64 years and half of this period corresponds to peak fertility and child-bearing years.

Retinopathy has been reported in 18-41% of pregnant diabetics[6]. More recent studies reported the incidence to be 47%[15] and 77%[16]. In our study the incidence was 58% for the pregnant diabetics and 30% for the controls. The increased incidence could be related to more patients attending antenatal clinics and better antenatal care.

Progression of DR was reported in 3-29% of diabetic pregnant patients[17]. In our study progression occurred in 28.6%(10/35) of pregnant patients who had retinopathy at first visit. 15% of background diabetic retinopathy and 46.6% of PDR showed progression of their disease. Rodman reported that 10% of BGDR and 25% of PDR progress during pregnancy[18]. Its now generally understood that BGDR may wax and wane in either pregnant or non-pregnant state and that temporary exacerbation to a more severe state of BGDR during pregnancy usually stabilizes or reverts to the pre-pregnancy status following delivery. Unfortunately if BGDR progresses to severe PDR during pregnancy, the retinal changes are less likely to regress following delivery. Remission of PDR due to previous laser treatment tends to protect the eyes during pregnancy, and this was found in our study where progression in untreated group of PDR occurred in 62.5% while it occurred in 29% of treated group. It was reported that in women with IDDM and no retinopathy, pregnancy doesn't appear to induce or worsen this complication[18], although there was one reported case of development of PDR with gestational diabetes without prior history of the disease[19].

In our study we found that the duration of Diabetes Mellitus (DM) is the only significant factor in development and progression of retinopathy. Moloney et al had previously reported that every pregnant patient who had had diabetes for more than ten years has retinopathy[9]. Another study reported that a patient who has DM for 15 years has 63% chance of having DR, 18% chance of having PDR, and 2% chance of being totally blind[20].

Laser photocoagulation is the treatment of choice for PDR and it is as efficient during pregnancy as in a non-pregnant patient, where its destruction of peripheral retina decreases the total retinal metabolic demand, thus decreasing the hypoxic drive of neovascularization in the remaining living retina.

In the past it was advised to terminate pregnancy in the presence of severe PDR, but it was found that with appropriate management a history of PDR is not a contraindication to pregnancy in patients who do not have other serious complications of diabetes, but careful pre-pregnancy counseling should be offered to such patients[21]. However, an additional consideration in women with active PDR at the end of pregnancy, is the route of delivery. Since traction stresses can rupture vessels proliferating into the vitreous, these patients are advised not to strain while under treatment; for this reason Caesarean

section is advised for women with active PDR in order to avoid the Valsava manoeuver in the second stage of labour.

CONCLUSION

Diabetic patients should be better informed about the effectiveness of timely treated diabetic retinopathy because duration of diabetes was the most important risk factor related to retinopathy, and the need for regular ophthalmologic follow-up during pregnancy to stabilize or revert the changes to the pre-pregnancy status.

REFERENCES

1. Kahn HA, Bradley RF. Prevalence of diabetic retinopathy. Br J Ophthalmol 1979;59:345.
2. Kitzmiller JL, Aiello LM, Kaldany A, et al. Diabetic vascular disease complicating pregnancy. Clin Obstet Gynecol 1981;24:107-23.
3. Reece EA, Homko CJ, Hagay Z. Diabetic retinopathy in pregnancy. Obstet Gynecol North Am 1996;23:161-71.
4. Beetham WB. Diabetic retinopathy in pregnancy; Trans Am Ophthalmol Soc 1950;48:205.
5. Burt RL, Weaver RG. Proliferative diabetic retinopathy in pregnancy. Obstet Gynecol 1979;40:199.
6. Cassar J, Kohner EM, Hamilton AM, et al. Diabetic retinopathy and pregnancy. Diabetoloia 1978;15:105.
7. Walender PE, Wadman B, Andersson L, et al. Pregnancy and diabetic retinopathy. Acta ophthalmol 1971;120:66.
8. Axer –Siegel R, Hod M, Fink-Kohen S, et al. Diabetic retinopathy during pregnancy. Ophthalmology 1996;103:1815-19.
9. Moloney JB, Drury MI. The effect of pregnancy on the natural course of diabetic retinopathy. Am J Ophthalmol 1982;93:745-56.
10. Soubrane G, Canivet J, Coscas G. Influence of pregnancy on the evolution of background retinopathy. Preliminary results of a prospective fluorescein angiography study. Int Ophthalmol 1998;8:249-55.
11. Pedersen J. The pregnant diabetic and her newborn. Munksgaard 1977:97.
12. Aimer LO, Pandolf M. Fibrinolysis and diabetic retinopathy. Diabetes 1976;25:807.
13. Larinkari J, Laatikainen L, Ranta T, et al. Metabolic control and serum hormone levels in relation to retinopathy in diabetic pregnancy. Diabetologia 1982;22:327-32.
14. Sono H, Okuda Y, Kawakami Y, et al. Progesterone induces vascular endothelial growth factor on retinal pigment epithelial cells in culture. Life Sci 1996;59:21-5.
15. Hovart M, MacLean H, Goldberg L, et al. Diabetic retinopathy in pregnancy, a twelve year prospective study. Br J Ophthalmol 1980; 64:398-403.
16. Ugoleva SV, Baranov VG, Koshelva NG. The course of pregnancy and diabetes

mellitus in pregnant women with a long-standing disease. Prob Endocrinol 1982;28:6-10

17. Rodman HM, Singerman LJ, Aiello LM, et al. Diabetic retinopathy and its relation to pregnancy. The diabetic pregnancy and perinatal perspective. In: Merkatz TR, Adams PAJ, eds. New York, Grune and Stratton:1979.
18. Lapolla A, Cardone C, Negrin P, et al. Pregnancy does not induce or worsen retinal and peripheral nerve dysfunction in insulin dependant diabetic women. J Diab Complications 1998;12:74-80.
19. Hagay Z, Schachter M, Pollack A, et al. Development of proliferative retinopathy in a gestational diabetes patient following rapid metabolic control. Eur J Obstet Gynecol Reprod Biol 1994;57:211-3.
20. Verougstaete C. Diabetic retinopathy and pregnancy. Bull Soc Belge Ophthalmol 1995;256:33-41.
21. Price JH, Hadden DR, Archer DB, et al. Diabetic retinopathy in pregnancy. Br J Obstet Gynecol 1984;91:11-17.