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## **Academic Dissertation**

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## **DIABETIC RETINOPATHY AND PREGNANCY**

### **ABSTRACT**

The purpose of the present prospective study was to gain better understanding about the characteristics and pathogenetic mechanisms of diabetic retinopathy (DR) during pregnancy in women with type I diabetes. The aim was to compare retinal capillary blood flow in women with type I diabetes with nondiabetic control women during pregnancy and postpartum and with nonpregnant diabetic women using two different methods. The hypothesis was that progression of DR during pregnancy is associated with increased retinal capillary blood flow in diabetic women (I, II).

The third study was carried out to reveal whether macular topographical changes occur in diabetic compared to nondiabetic women during pregnancy and postpartum. In addition, the loss of contrast sensitivity (CS) was suspected of being related to macular thickening during diabetic pregnancy. The fourth study was carried out to evaluate the role of various systemic vasoactive mediators in the development or progression of DR during pregnancy and postpartum. The fifth study aimed to clarify the role of various systemic angiopoietic factors in the development or progression of DR during pregnancy and postpartum.

Firstly, in a prospective sub-study of 46 pregnant women with diabetes and 11 nondiabetic pregnant women macular capillary blood flow velocity was measured by psychophysical blue-field entoptic simulation test. In diabetic women, the macular capillary blood flow velocity was higher than in nondiabetic women throughout pregnancy and postpartum. Further, capillary blood flow velocity seemed to depend on the grade of DR. Diabetic women with no or very mild retinopathy had lower macular capillary blood flow velocities than those with more severe retinopathy, but higher velocities than nondiabetic women. A temporal increase from the first trimester to the postpartum period was observed in diabetic but not in nondiabetic women. These data supported the concept that capillary hyperperfusion may play a role in the development of DR during pregnancy.

Secondly, perimacular capillary blood flow was measured in 32 pregnant women with type I diabetes and 11 nondiabetic pregnant women by confocal laser Doppler flowmetry throughout pregnancy and postpartum in a prospective sub-study (II). The flow values were higher in diabetic women during pregnancy, compared to nondiabetic pregnant women or nonpregnant diabetic women. In diabetic women with mostly minimal to moderate retinopathy, no clear correlation between flow values and progression of DR could be observed. These results indicated that retinal capillary blood flow responds to pregnancy in a different manner in diabetic women compared to nondiabetic women, which may be related to impaired autoregulation of capillary blood flow in diabetes.

Thirdly, in a prospective sub-study of 46 diabetic women and 11 nondiabetic controls macular surface topography was measured by confocal scanning laser tomography throughout pregnancy and postpartum (III). In diabetic women, especially in those with clear progression of DR, the macula was slightly more elevated than in nondiabetic controls. Furthermore, CS was lower in diabetic than in nondiabetic women at mid-spatial

frequencies, and loss of CS was correlated with macular elevation during the third trimester in diabetic women even in the absence of retinopathy.

Fourthly, in a prospective sub-study of 53 pregnant diabetic and 9 nondiabetic women DR was graded from fundus photographs (IV). Plasma markers of renin-angiotensin-system (RAS) (plasma renin activity, angiotensin II, aldosterone), natriuretic peptides (ANP, BNP, CNP), and adrenomedullin were measured during the first and third trimesters, and at 3 months postpartum. Diabetic pregnancy was associated with lower levels of PRA and ANP compared to nondiabetic pregnancy. But no clear associations between the vasoactive hormones and progression of retinopathy could be detected.

Fifthly, in a prospective sub-study of 26 pregnant women with type I diabetes and 8 nondiabetic controls plasma levels of angiopoietin-1 and -2, hVEGF-A and total soluble VEGF receptor-1 were measured during the first and third trimesters, and at 3 months postpartum (V). Levels of Ang-2 were lower in the diabetic than in nondiabetic women during pregnancy. At baseline, levels of angiopoietic factors showed no correlation with severity of DR. At 3 months postpartum, hVEGF-A levels were lowest in diabetic women with progression of retinopathy. The circulating levels of angiopoietic factors appeared not to be connected with the progression of retinopathy during pregnancy.

**Public discussion:** by the permission of the Medical Faculty of the University of Helsinki, in the Auditorium of the Department of Ophthalmology, Haartmaninkatu 4 C, Helsinki, on December 12<sup>th</sup>, 2003, at 12 o'clock noon.

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