



RESEARCH: COMPLICATIONS

Prevalence and severity of diabetic retinopathy in pregnant women with diabetes—time to individualize photo screening frequency

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Abstract

Aims: To evaluate the prevalence and severity of diabetic retinopathy including macular oedema in pregnant women with diabetes and to identify women in whom the frequency of retinal screening can be reduced to minimize the burden of health care visits.

Methods: A cohort study of 348 women with pre-existing diabetes were routinely screened with retinal photo in early (12 weeks) and late pregnancy (27 weeks). Diabetic retinopathy was classified in five stages in accordance with National Danish Guidelines based on the eye with the highest retinopathy level. Sight-threatening retinopathy was defined as the presence of proliferative retinopathy and/or clinically significant macular oedema (CSMO).

Results: Retinopathy was present in 52% (116/223) vs. 14% (17/125), with sight-threatening retinopathy in 16% (35/223) vs. 6% (7/125) of women with type 1 and type 2, respectively. Women without retinopathy in early and late pregnancy were characterized by shorter diabetes duration ($p < 0.0001$ and $p = 0.008$) and predominance of type 2 diabetes. Amongst the 50% (175/348) of the cohort having no retinopathy in early pregnancy and HbA1c < 53 mmol/mol (7.0%), none developed sight-threatening retinopathy and 94% (165/175) remained without any retinopathy during pregnancy. Development of sight-threatening retinopathy was mainly observed in women with retinopathy in early pregnancy. Treatment for sight-threatening retinopathy was given to a minority (2.7 and 2.4%, respectively).

Conclusion: Good glycaemic control and no retinopathy was seen in a large proportion of women in early pregnancy and none of these women developed sight-threatening retinopathy. The frequency of retinal screening can probably be safely reduced during pregnancy in these women.

KEYWORDS

diabetic retinopathy, macular oedema, pregnancy, type 1 diabetes, type 2 diabetes

1 | INTRODUCTION

Historically diabetic retinopathy has been the leading cause of acquired blindness in young and middle-aged adults.¹ However, consistent with improved diabetes management and routine retinal photo screening, diabetic retinopathy is no longer the leading cause of certifiable blindness.^{2,3}

Pregnancy, poor glycaemic control, and long diabetes duration increase the risk of development and progression of retinopathy.⁴⁻¹⁰ Sight-threatening diabetic retinopathy includes both proliferative retinopathy and clinically significant macular oedema (CSMO).¹¹ The prevalence of retinopathy in pregnant women with type 1 and type 2 (pre-existing) diabetes varies from 8% to 63%,^{4,8,11-15} but the prevalence of macular oedema and sight-threatening retinopathy requiring treatment during pregnancy is sparsely described in the literature.¹⁴ In recent years, glycaemic control in adolescents with type 1 diabetes has improved and the prevalence of retinopathy has declined considerably.¹⁶ Better glycaemic control in early life and subsequently during pregnancy may lead to a reduced prevalence of retinal changes during pregnancy.

The British¹⁷ and American¹⁸ guidelines still recommend at least two screenings for retinopathy in pregnancy, and the Danish Ophthalmological Society recommends retinal examination early in pregnancy, at 24–28 weeks and more frequently if indicated in women with pre-existing diabetes. However, retinal examinations are often stressful for women and increase the burden of being pregnant with diabetes. Both American¹⁸ and Danish¹⁹ guidelines now suggest that retinopathy screening beyond early pregnancy may be omitted in women without retinopathy and with good glycaemic control in early pregnancy, despite lack of solid evidence.

We hypothesized that in women without retinopathy in early pregnancy development of sight-threatening retinopathy during pregnancy would be rare. We aimed to evaluate the prevalence and severity of diabetic retinopathy including macular oedema in pregnant women with diabetes and to identify women in whom the frequency of retinal screening can be reduced to minimize the burden of health care visits.

2 | MATERIALS AND METHODS

2.1 | Study design

This is a secondary analysis of a prospective observational cohort study focusing on preeclampsia in pregnant women with pre-existing diabetes²⁰ where retinopathy status was

Novelty statement

- In recent years, glycaemic control has improved and led to a considerable decline in the prevalence of retinopathy during pregnancy. This may influence future retinal screening strategy.
- Almost half of the women with type 1 diabetes and the majority with type 2 diabetes did not have retinopathy in early pregnancy. If good glycaemic control was present in early pregnancy, none of these women developed sight-threatening retinopathy during pregnancy.
- The implication is that further photo-screening beyond early pregnancy might be postponed until post-partum in women with no retinopathy and good glycaemic control in early pregnancy.

routinely evaluated in early pregnancy, at 24–28 weeks and more frequently if indicated. Detailed retinal examination of women with retinopathy during pregnancy in the cohort was collected retrospectively.

2.2 | Subjects

Women with pre-existing diabetes referred <20 weeks with a singleton pregnancy to the Center for Pregnant Women with Diabetes at Rigshospitalet from September 2015 to February 2020 were offered inclusion. Exclusion criteria were age <18 years, insufficient Danish language skills, participation in the study in a previous pregnancy and severe concomitant diseases. In the current study, women with less than two available retinal screenings in pregnancy were excluded.

In total, 565 women were eligible for inclusion, whereof 468 (83%) accepted participation. In total, 120 women were excluded due to: abortion ($n = 26$), withdrawal of consent ($n = 31$), change in hospital ($n = 1$) or less than two available retinal screenings ($n = 62$), leaving 348 included women in the current study.

2.3 | Retinal screening—diabetic retinopathy and macula oedema

Retinal screening and visual acuity were planned at 12 weeks (early pregnancy) and at 27 weeks (late

pregnancy). The women with severe non-proliferative retinopathy, proliferative retinopathy or CSMO were further examined by repeated photo screening or by an ophthalmologist, when indicated. Visual acuity was evaluated with the Snellen chart, and impaired visual acuity was classified as below 0.8. At the eye examination in early and late pregnancy, five fundus photographs were taken routinely, making a mosaic of the five photographs, which was then screened, and optical coherence tomography (OCT) was performed. If no retinopathy was present at the first examination, the second eye examination was restricted to central photography and an OCT. A Topcon Triton OCT or Topcon Fundus Camera TRC-NW8 in combination with a Topcon OCT 2000 was used for the eye examinations. The severity of retinopathy in a woman was based on the highest documented level in these screenings.

Diabetic retinopathy was classified in five stages in accordance with National Danish Guidelines²¹ using a slightly modified version of the 'Proposed International Clinical Diabetic Retinopathy severity scale' by Wilkinson²²:

1. No diabetic retinopathy: No diabetes-induced retinal abnormalities.
2. Mild non-proliferative diabetic retinopathy (NPDR): Microaneurysms/single punctiform haemorrhages.
3. Moderate NPDR: More than just microaneurysms/punctiform haemorrhages but less than severe NPDR.
4. Severe NPDR: Involves at least one of the following changes:
5. More than 20 intraretinal haemorrhages in each of the four retinal quadrants.
6. Venous beading in at least two retinal quadrants.
7. Significant intraretinal microvascular abnormalities (IRMA) in at least one retinal quadrant.
8. Proliferative diabetic retinopathy: Pre-retinal vascular proliferation, diabetes-induced vitreous haemorrhage, or signs of previous pan-retinal laser treatment (including both stable and active previously laser-treated proliferative retinopathy).

Diabetic macular oedema was classified into three stages²¹:

1. No diabetic macular oedema: None of the listed criteria below.
2. Diabetic macular oedema: Diabetes-induced retinal thickening and/or hard exudates within 1 disc diameter from the macular centre.
3. Clinically significant diabetic macular oedema (CSMO): Involves at least one of the following changes:

4. Retinal thickening within 500 μm distance from the centre of the macula.
5. Hard exudates within 500 μm distance from the centre of the macula with adjacent retinal thickening.
6. Retinal thickening >1 papilla area with any part of the thickened area placed <1 papilla's diameter from the macula centre.

Indications for laser treatment of proliferative retinopathy were based on the local ophthalmologist's (JNH) decision and given when progression or new onset was documented. CSMO was generally observed without intervention, however, when CSMO was combined with clinically significantly impaired visual acuity treatment with dexamethasone intravitreal implant could be given²³ whilst anti-vascular endothelial growth factor agents generally were avoided.

In the current study, retinopathy status was divided into three groups: No retinopathy, non-proliferative retinopathy (NPDR and/or diabetic macular oedema) and sight-threatening retinopathy (proliferative retinopathy and/or CSMO).

2.4 | Routine diabetes care

The women followed the routine care program for pregnant women with pre-existing diabetes as described previously^{20,24} and given in short below.

The women attended obstetrical and diabetes appointments regularly. Blood pressure (BP), weight and HbA1c was registered at each visit, and sterile urine was screened for proteinuria with a urine dipstick test. Furthermore, insulin dose, antihypertensive treatment, and the number of mild hypoglycaemic events (defined as symptoms familiar to the woman as hypoglycaemia and managed by her²⁵) were noted.

On 23 February 2018, targets for glycaemic control changed slightly: HbA1c targets changed from <50 mmol/mol (6.7%) to <48 mmol/L (6.5%) before 20 weeks and from <40 mmol/mol (5.8%) to <38 mmol/L (5.6%) thereafter. Plasma glucose targets changed from 4–6 mmol/L to 4–5.5 mmol/L preprandially and from 4–8 to 4–7 mmol/L postprandially. Blood glucose monitoring was recommended before and 90 min after meals as well as before bedtime.

Diabetic nephropathy was determined based on two urine samples when available including microalbuminuria and known pre-existing nephropathy.^{11,26} Chronic hypertension (without kidney involvement) was defined as pre-pregnancy hypertension or newly detected office BP $\geq 135/85$ mmHg with home BP $\geq 130/80$ mmHg in early pregnancy.²⁴

Preeclampsia was defined as BP \geq 140/90 mmHg measured twice occurring after 20 weeks accompanied by proteinuria (\geq 1+) and/or new onset of symptoms of organ dysfunction.²⁴ In women with diabetic nephropathy, an additional increase in systolic or diastolic BP by \geq 15% was needed.²⁴

Before 23 February 2018, selected women with additional risk factors for preeclampsia were recommended aspirin from 10 weeks. After this date, all women were recommended aspirin and, in case of vitamin D insufficiency, vitamin D supplements.²⁰

2.5 | Statistical analyses

Data were given as a number (%), mean \pm SD or median (interquartile range) when appropriate. For comparison of women with and without retinopathy χ^2 -test, Fisher's exact test and unpaired *t*-test or Mann-Whitney U test were used as appropriate (women with non-proliferative retinopathy and sight-threatening retinopathy were combined). Multiple imputations of missing data was not used. Data on women with retinopathy divided into non-proliferative retinopathy or sight-threatening retinopathy and the grading of each eye were evaluated with descriptive statistics only, due to relatively low numbers. A two-sided *p*-value $<$ 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 25 (IBM Corp., Armonk, NY, USA).

The study was approved by The National Committee on Health Research Ethics (H-15019186) and The Danish Data Protection Agency (2012-58-0004, RH-2015-289, I-Suite: 04305), and was in accordance with the Helsinki declaration. Written informed consent was obtained from all participants. In women where implantation of dexamethasone intravitreally was found indicated due to large oedema and considerable vision loss, information of advantages and disadvantages of the treatment were given, and informed consent was obtained.

3 | RESULTS

In total, 348 women had retinal examinations performed at 12 (10-15) and 27 (27-29) weeks, hereof 223 women with type 1 diabetes and 125 with type 2 diabetes.

Women with type 1 diabetes had a longer diabetes duration ($p <$ 0.0001) and a higher prevalence of diabetic retinopathy ($p <$ 0.0001) and macular oedema ($p =$ 0.01) in early pregnancy compared with women with type 2 diabetes (Table 1). Women with type 1 and type 2 diabetes are therefore described separately below.

In women with type 1 diabetes, there were 52% (116/223) with retinopathy in pregnancy and 48% without. Women with retinopathy were characterized by a longer diabetes duration ($p <$ 0.0001), and of higher prevalence of mild hypoglycaemia ($p =$ 0.02) and chronic hypertension ($p =$ 0.0002), compared with those without retinopathy, whereas HbA1c was comparable between both groups (Table 2). Sight-threatening retinopathy was present in 16% (35/223). Amongst 20 women diagnosed with proliferative diabetic retinopathy, 16 had prior laser treatment for proliferative retinopathy, whereof two (0.9%) received additional laser treatment for progression, whilst four were treatment naïve and continued so during pregnancy. Four (1.8%) women received dexamethasone intravitreal implant for CSMO with impaired visual acuity.

In women with type 2 diabetes, there were 14% (17/125) with retinopathy and 86% (108/125) without. Women with retinopathy were characterized by longer diabetes duration ($p =$ 0.008), higher HbA1c in early pregnancy ($p <$ 0.0001) and a higher prevalence of diabetic nephropathy ($p =$ 0.008) compared with those without retinopathy (Table 2). Sight-threatening retinopathy was present in 6% (7/125). Amongst three women with proliferative diabetic retinopathy, two had prior laser treatment, whereof one (0.8%) received additional laser treatment for progression. One woman developed proliferative retinopathy and was left untreated. Two women (1.6%) received dexamethasone intravitreal implant for CSMO with impaired visual acuity.

In type 1 diabetes, proliferative retinopathy was present in 7% (30/446) of the individual eyes in early pregnancy and additionally five (1%) eyes progressed to proliferative retinopathy during pregnancy. CSMO was present in 5% (23/446) of the individual eyes in early pregnancy and additionally, 9 (2%) eyes developed CSMO during pregnancy. Amongst 20 eyes with CSMO in early pregnancy and left untreated, 50% (10/20) regressed spontaneously to no macular oedema.

In type 2 diabetes, proliferative retinopathy was present in 2% (4/250) of the individual eyes in early pregnancy and additionally, one eye (0.4%) progressed to proliferative retinopathy. CSMO was not present in early pregnancy and 1% (3/250) of the individual eyes progressed to CSMO during pregnancy.

Forty-two% (94/223) of the women with type 1 diabetes and 65% (81/125) of the women with type 2 diabetes had HbA1c $<$ 53 mmol/mol (7.0%) and no retinopathy in early pregnancy. This accounted for 50% (175/348) of the women with pre-existing diabetes in total.

Based on the above findings the following sub-analysis was performed in women with type 1 or type 2 diabetes combined. Amongst women without retinopathy and HbA1c $<$ 53 mmol/mol (7.0%) in early pregnancy none developed

TABLE 1 Clinical characteristics at inclusion and 36 weeks in 348 pregnant women with type 1 and type 2 diabetes

	All women (n = 348)	Type 1 diabetes (n = 223)	Type 2 diabetes (n = 125)	p-value (type 1 vs. type 2 diabetes)
Maternal age (years)	32 ± 5	31 ± 5	34 ± 5	<0.0001
Duration of diabetes (years)	11 (3–18)	16 (10–22)	3 (1–7)	<0.0001
Pre-pregnancy BMI (kg/m ²)	26.9 (23.3–32.3)	24.6 (22.2–28.7)	32.3 (27.6–37.4)	<0.0001
Northern European origin	265 (77)	201 (92)	64 (52)	<0.0001
Smoking	21 (6)	15 (7)	6 (5)	0.46
HbA1c at inclusion				0.98
mmol/mol	46 (42–53)	47 (43–52)	46 (42–54)	
%	6.4 (6.0–7.0)	6.5 (6.1–6.9)	6.4 (6.0–7.1)	
HbA1c at 36 weeks				0.0003
mmol/mol	41 (38–46)	42 (38–46)	39 (36–44)	
%	5.9 (5.6–6.4)	6.0 (5.6–6.4)	5.7 (5.4–6.2)	
Diabetic retinopathy in at least one eye in early pregnancy	118 (34)	102 (46)	16 (13)	<0.0001
Non-proliferative diabetic retinopathy	99 (28)	85 (38)	14 (11)	
Proliferative diabetic retinopathy	19 (6)	17 (8)	2 (2)	
Previous laser-treated proliferative diabetic retinopathy in early pregnancy	18 (5)	16 (7)	2 (2)	0.02
Macular oedema in at least one eye in early pregnancy	31 (9)	26 (12)	5 (4)	0.01
Diabetic macular oedema ^a	16 (5)	11 (5)	5 (4)	
Clinically significant macular oedema	15 (4)	15 (7)	0 (0)	
Sight threatening retinopathy in early pregnancy ^b	30 (9)	28 (13)	2 (2)	0.0005
Diabetic nephropathy	23 (7)	13 (6)	10 (8)	0.45
Chronic hypertension ^c	36 (11)	13 (6)	23 (20)	0.0001
Systolic blood pressure at inclusion (mmHg)	119 ± 12	117 ± 11	123 ± 12	<0.0001
Diastolic blood pressure at inclusion (mmHg)	76 ± 8	75 ± 7	79 ± 8	<0.0001

Note: Data are expressed as number (%) and mean ± SD or median (interquartile range) depending on the distribution. Data were obtained from 92%–100% of the women unless otherwise stated.

^aDiabetic macular oedema denotes macular oedema without clinically significant macular oedema.

^bProliferative diabetic retinopathy and/or clinically significant macular oedema in at least one eye.

^cPre-existing hypertension or newly detected hypertension before 20 weeks, not including women with diabetic nephropathy.

sight-threatening retinopathy and 94% (165/175), remained without retinopathy. In women without retinopathy and HbA1c ≥53 mmol/mol (7.0%) in early pregnancy, none developed proliferative retinopathy and 2% (1/55) developed CSMO requiring treatment, whilst 93% (51/55) remained without retinopathy. Amongst women with mild retinopathy in early pregnancy development of sight-threatening retinopathy occurred in 8% (4/49).

The 62 women excluded due to missing retinal examinations in early or late pregnancy were comparable to the included women with 34 having type 1 diabetes and 28 having type 2 diabetes with a diabetes duration of 12 years (7–20) and 4 years (1–7), respectively, and HbA1c 48 mmol/mol (45–53) (6.5% [6.3–7.0%]) and 47 mmol/mol (41–52) (6.5% [5.9–6.9%]) in early pregnancy, respectively.

TABLE 2 Clinical characteristics in 223 women with type 1 diabetes and 125 women with type 2 diabetes according to retinopathy classification during pregnancy

	Type 1 diabetes				Type 2 diabetes			
	Retinopathy		Retinopathy		Retinopathy		Retinopathy	
	No retinopathy (n = 107)	NPDR (n = 81)	PDR and/or CSMO (n = 35)	p-value ^a	No retinopathy (n = 108)	NPDR (n = 10)	PDR and/or CSMO (n = 7)	p-value ^a
Maternal age (years)	31 ± 5	30 ± 5	33 ± 5	0.99	34 ± 5	32 ± 4	33 ± 3	0.19
Duration of diabetes (years)	10 (6–17)	18 (14–21)	24 (19–28)	<0.0001	2 (1–6)	8 (3–13)	7 (2–10)	0.008
Pre-pregnancy BMI (kg/m ²)	24.4 (22.3–28.5)	25.0 (22.4–29.6)	24.4 (21.8–28.1)	0.48	32.1 (27.6–36.7)	36.5 (30.6–41.3)	32.4 (24.8–35.4)	0.44
Northern European origin	97 (92)	73 (94)	31 (89)	0.89	58 (54)	5 (50)	1 (14)	0.15
Smoking	8 (8)	5 (7)	2 (6)	0.66	6 (6)	0 (0)	0 (0)	1.0
HbA1c at inclusion								
mmol/mol	46 (42–52)	47 (43–52)	48 (43–54)	0.14	45 (41–53)	64 (53–71)	59 (50–70)	<0.0001
%	6.4 (6.0–6.9)	6.5 (6.1–6.9)	6.5 (6.1–7.1)		6.3 (5.9–7.0)	8.0 (7.0–8.6)	7.5 (6.7–8.6)	
HbA1c at 36 weeks								
mmol/mol	42 (38–46)	42 (38–47)	43 (40–45)	0.58	39 (36–44)	44 (39–54)	42 (40–44)	0.02
%	6.0 (5.6–6.4)	6.0 (5.6–6.5)	6.1 (5.8–6.3)		5.7 (5.4–6.2)	6.2 (5.7–7.1)	6.0 (5.8–6.2)	
Decrease in HbA1c from inclusion to 36 weeks								
mmol/mol	3 (0–8)	5 (0–10)	5 (0–13)	0.25	5 (1–13)	17 (8–26)	16 (7–25)	0.001
%	0.3 (0–0.7)	0.5 (0–0.9)	0.5 (0–1.2)		0.5 (0.1–1.2)	1.6 (0.7–2.4)	1.5 (0.6–2.3)	
Number of mild hypoglycaemic events at inclusion (number/week)	6 (3–10)	7 (4–13)	7 (6–14)	0.02	0 (0–0)	0 (0–2)	0 (0–7)	0.49
Insulin pump therapy	34 (32)	34 (42)	14 (40)	0.14	0 (0)	0 (0)	0 (0)	-
Diabetic nephropathy	2 (2)	5 (6)	6 (16)	0.05	6 (6)	2 (20)	2 (29)	0.008
Chronic hypertension	0 (0)	5 (7)	8 (28)	0.0002	20 (20)	0 (0)	3 (60)	0.72
Systolic BP at inclusion (mmHg)	116 ± 11	117 ± 9	121 ± 13	0.19	122 ± 13	124 ± 6	126 ± 10	0.21
Diastolic BP at inclusion (mmHg)	74 ± 7	75 ± 7	76 ± 8	0.12	79 ± 8	80 ± 5	80 ± 10	0.59
Prophylactic aspirin	67 (63)	49 (61)	28 (80)	0.56	48 (44)	3 (30)	6 (86)	0.51
Preeclampsia	6 (6)	12 (15)	5 (14)	0.03	10 (9)	0 (0)	3 (43)	0.38

Note: Data are expressed as number (%) and mean ± SD or median (interquartile range) depending on the distribution.

Abbreviations: BP, blood pressure; CSMO, clinically significant macular oedema; DMO, diabetic macular oedema without CSMO; DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

^aNo DR versus (NPDR and PDR/CSMO).

4 | DISCUSSION

In this cohort study including 348 women with pre-existing diabetes, retinopathy during pregnancy was present in 52% of the women with type 1 diabetes and in 14% of the women with type 2 diabetes. Sight-threatening retinopathy requiring treatment was rare and did not develop in women without retinopathy and with good glycaemic control in early pregnancy.

The prevalence of retinopathy in early pregnancy amongst women with type 1 diabetes in the present study was numerically lower than the 63% found in a previously published study in 2010 covering the same geographical area¹¹ and the prevalence during pregnancy compared to a recent French study in 499 pregnancies.¹²

In the present study, HbA1c in early pregnancy was slightly lower than HbA1c in early pregnancy of 50 mmol/mol (6.7%) in our previous study,¹¹ which may indicate a general improvement in glycaemic control over the last decade explaining the slightly lower prevalence of retinopathy in the present study compared with our previous cohort.¹¹ Improved glycaemic control and a decline in retinopathy amongst adolescents with type 1 diabetes in recent years¹⁶ may also lead to a reduced prevalence of retinopathy during pregnancy.

The prevalence of women requiring laser treatment in the present study was comparable or lower than the prevalence of 3.7% in women with type 1 diabetes¹¹ and 4% in women with type 2 diabetes²⁷ previously reported in the two other cohorts from our centre.

Our study is the first large cohort study describing the prevalence and changes in macular oedema during pregnancy in both type 1 and type 2 diabetes. In almost half of the eyes with CSMO in early pregnancy, macular oedema regressed spontaneously, as also seen outside of pregnancy.²⁸ In a few cases, CSMO was combined with clinically significantly impaired visual acuity and treated with dexamethasone intravitreal implant²³ whilst anti-vascular endothelial growth factor agents generally were avoided as also recommended in a recent review.²⁹ These women were followed for possible changes in intraocular pressure and/or cataract formation. The systemic dexamethasone concentration was considered small and safe for the fetus.

Elevated HbA1c levels in early pregnancy have previously been associated with the development and progression of retinopathy,^{12,30,31} however, in the present study most women with type 1 diabetes had good glycaemic control and HbA1c was only associated with the presence of retinopathy in women with type 2 diabetes. In accordance with previous studies, diabetes duration was an important risk factor for the presence of retinopathy.^{11-14,31}

Our findings are in accordance with the previous studies^{12,14} where progression of retinopathy was most common in the first and second trimester, and rare if no retinopathy was present in early pregnancy. A review³¹ based on small observational studies concluded that first-trimester retinal examination should be performed in all women with pre-existing diabetes and if no retinopathy was found, it was proposed to delay further retinal examination until postpartum in most cases unless poor glycaemic control was present. However, the evidence for this statement does not seem solid since the glycaemic control was not taken into account in previous cohort studies.^{12,14} Our study of a large, unselected cohort provides evidence for a very low risk of developing sight-threatening retinopathy during pregnancy if the women have no retinopathy and good glycaemic control in early pregnancy. Mild retinopathy in early pregnancy did not seem to be associated with similar low risk.

We found that chronic hypertension was associated with retinopathy, in accordance with some,^{7,31} but not all studies.^{12,15}

The low prevalence of retinopathy, particularly proliferative retinopathy, amongst women with type 2 diabetes in the current study is in accordance with our previous study²⁷ and studies describing the prevalence of macular oedema were not found.

The strength of this study was the evaluation of both diabetic retinopathy and macular oedema and whether treatment for sight-threatening retinopathy was given in a large cohort including both women with type 1 and type 2 diabetes. We generally used a mosaic of five fundus photographs, but we cannot rule out a small risk of overlooking retinal changes in the overlaps that may impact the retinopathy grading. Amongst women without retinopathy in the first five fundus photographs, the simplified second examination may have overlooked newly developed isolated changes in the periphery. Unfortunately retinal evaluation of possible changes in retinopathy after delivery was not available, but the progression of retinopathy the year after pregnancy has been described to be low (4%) compared to progression during pregnancy (22%).¹²

Management of pre-existing diabetes during pregnancy imposes a lot of extra daily challenges on the women and frequent hospital visits. Therefore, it seems reasonable to individualize their antenatal care programs and reduce the amount of unnecessary hospital visits as proposed in international guidelines.^{18,19} This paper is the first to validate a safe and pragmatic method for selecting pregnant women for reduced screening frequency. This approach with individualized retinal examinations is also seen in the non-pregnant population of persons with diabetes where a longer follow up of two to three years before re-screening has been suggested

if they have no retinopathy.³² The clinical implication of this study may involve a change in practice with a delay of further retinal examinations to post-partum if no retinopathy is found at the first retinal examination during pregnancy and good glycaemic control defined as HbA1c <53 mmol/mol (7.0%) is present in early pregnancy. Based on the findings of the present study, approximately 50% of photo screenings in late pregnancy would thus no longer be necessary at our centre. Regular screening of women with mild to severe retinal changes in early pregnancy is still advisable.

5 | CONCLUSION

Good glycaemic control and no retinopathy was seen in a large proportion of women in early pregnancy and none of these women developed sight-threatening retinopathy. The frequency of retinal screening can probably be safely reduced during pregnancy in these women.

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CONFLICTS OF INTEREST

None to declare.

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