



Risk factors for diabetic retinopathy

Diabetic retinopathy is the leading cause of working age blindness in the developed world. After 20 years of disease, nearly all type 1 diabetics and greater than 60 per cent of patients with type 2 diabetes have retinopathy.¹ There are many proposed risk factors and treatments associated with diabetic retinopathy in the literature, but evidence is needed to establish their relative importance. Education on risk factors and intervention options available may help us to make better choices to prevent the onset and manage this condition, ultimately leading to less sight loss and a better quality of life.

Non-modifiable risk factors

Duration of diabetes

It is of note that it is the time since diagnosis independently of diabetes control which is the most important risk factor for developing some form of retinopathy.² A total of 2,366 diabetic patients participated in the famous Wisconsin Epidemiologic Study of Diabetic Retinopathy which found a strong link between duration of diabetes and presentation of retinopathy (Figure 1): 'the prevalence of retinopathy varied from 2 per cent in persons with less than two years of diabetes to 98 per cent in persons with 15 or more years of disease ... the severity of diabetic retinopathy was also related to duration of diabetes.'³

Bek *et al* published a reputable set of data, gathered from 5,365 diabetic

This is an edited extract from the 2012 winner of the *Optician/City University Prize for Best Dissertation*. **Michelle Sarah Barry** outlines the non-modifiable risk factors for diabetic retinopathy



Rex Features

Knowledge of risk factors for retinopathy is important for clinicians

patients over a period of more than 14 years at Aarhus University Hospital, who were involved in a standardised screening programme there.⁴ From their data, it can be seen that as the years go by from first examination of diabetes, progressively more diabetics go on to develop retinopathy that clinically requires treatment (regardless of type). Type 2 patients seemingly need treatment earlier in the disease than type 1 patients; however it is questionable whether type 2 diabetes is always diagnosed the same year as its onset.

Age of patient

Given the importance of disease duration, it follows that by the end of their lives, diabetic patients are more likely to have severe retinopathy. Certainly, older people are more likely to have diabetes. However, many have questioned whether age alone can be used to predict the stage of retinopathy. Klein⁵ is doubtful: 'the effect of disease duration is not uniform at all age...following puberty, age is not a significant predictor of retinopathy status in either insulin-dependent or non-insulin diabetic persons.'

While a review by Pinhas-Hamiel and Zeitler⁶ demonstrates a considerable rise in diabetes in

younger individuals over the last two decades, it is possible that their findings simply reflect an increased awareness, screening and therefore recording of diabetes (particularly in young people following associated media interest).

However, a thorough statistical analysis by Wong *et al*⁷ of 14,074 type 2 patients provides a strong argument that 'age of diagnosis is an independent predictor of long-term retinopathy'. They looked at 624 patients with disease duration of 20-30 years, and 852 with disease duration 10-12 years, all referred to hospital in Sydney (Australia), and made statistical allowances for both hyperglycaemia and duration of diabetes. In the longer duration group, patients under the age of 45 (at age of diagnosis) had approximately three-times more retinopathy, and more sight-threatening retinopathy. Wong *et al* put forward an interesting hypothesis, that young people are more predisposed to hyperglycaemia and an aggressive response to VEGF, and thereby young (under age 45) people are more predisposed to retinopathy; this has not yet been proven.

Gender

Klein *et al*³ have stated that males are more at risk of retinopathy than

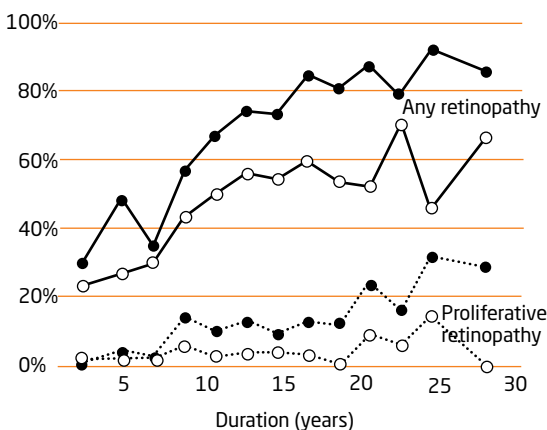


Figure 1 Percentage of patients with retinopathy as a function of diabetes duration. Black circles represent those not receiving insulin³



females: 'In the WESDR, younger-onset male patients with 10 or more years of diabetes were one and a third times more likely to have proliferative diabetic retinopathy (PDR) than younger-onset female patients with similar duration of disease.' Another large study⁴ strongly supports these findings; they show that men on average tend to require treatment earlier than women. There was less than a 5 per cent statistical chance that this is not the case for male Type I patients. Furthermore, the UK government figures show that male type 2 patients had a higher incidence of retinopathy than female type 2 patients.

The reason why males on the whole are more susceptible to retinopathy has not yet been established – one possibility is lifestyle differences.⁸ Although the evidence suggests men require treatment earlier on average, the disparity between the sexes is not especially large; this risk factor is less important than the age of the patient, and definitely less than disease duration.

Family history

Diabetes UK⁹ has published statistics on diabetes, which confirm that having two parents with diabetes significantly increases the risk of developing the condition. In type 1 diabetes the risk goes from 2 per cent (mother with condition) or 8 per cent (father with condition) to 30 per cent if both parents are affected. In type 2 diabetes the risk with one parent affected is 15 per cent, rising to 75 per cent if both parents are affected. Genetics seems likely to play a role in which offspring will become diabetic. However, not all children with diabetic parents will get this condition. It is possible that a diabetic 'lifestyle' (non-genetic factors such as lack of exercise and poor diet) may be confounding factors.

Ethnicity

According to Diabetes UK,⁹ type 2 diabetes is up to six times more common in people of South Asian descent and up to three times more common among people of African and African-Caribbean origin. Their published data on self-reported cases in England give a fuller picture (Table 1).

The Welsh Eye-Care Initiative (WECI) gives free eye tests to individuals considered at risk of certain eye diseases, including people who are of a particular race considered more at risk of diabetic retinopathy: Black-African, Black-Caribbean, Indian and

TABLE 1

Prevalence of men and women with diabetes, by minority ethnic group⁹

Minority ethnic group	Men	Women
Indian	10.1%	5.9%
Black Caribbean	10.0%	8.4%
Bangladeshi	8.2%	5.2%
Pakistani	7.3%	8.6%
Black African	5.0%	2.1%
General population	4.3%	3.4%
Chinese	3.8%	3.3%
Irish	3.6%	2.3%

Pakistani. From Table 1, this makes sense, especially for the Indian and Black-Caribbean populations, which have over twice the prevalence of diabetes as the general population.

Nephropathy

Kidney disease (nephropathy) is more common in diabetes, though until recently it was unclear whether nephropathy or diabetes was the cause or effect. Klein's analysis of the WESDR showed that in people with 10 or more years of diabetes, PDR was found two or three times as frequently in the presence of proteinuria [excess protein in urine due to bad filtering by kidneys] as in its absence.³

Glynn *et al*¹⁰ measured blood samples from the 1,441 participants of the Diabetes Control and Complications Trial (DCCT) and, based on their results, proposed that nephropathy may represent an early risk marker of long term complications in type 1 diabetics. These results hold merit, as the authors had adjusted results for several confounding variables including age, sex, duration of diabetes, and had randomised treatment assignment.

In 2010, findings were published based on the 15-year Beaver Dam Eye Study, in which over 3,000 people were examined. They showed that

nephropathy was a risk factor for new cases of retinopathy, as well as its severity. The authors point out that renal disease is associated with hypertension, inflammation, and endothelial dysfunction, all hypothesised as pathogenic factors for the development of retinopathy.¹¹

Hypothyroidism

The American Diabetes Association¹² performed a cross-sectional study, the underlying hypothesis of which was that there would be a link between poor thyroid function and diabetic retinopathy, because patients with subclinical hypothyroidism have an increase in cardiovascular events, as is often the case with diabetic patients. The results of the study showed a trend towards higher rates of sight-threatening diabetic retinopathy in a group of subclinical hypothyroid patients when compared with the 'euthyroid' (normally functioning thyroid gland) group. Given the 95 per cent confidence interval found, and the 1,170 type 2 patients looked at in the study, it is tempting to make a definitive link between poor thyroid function and level of diabetic retinopathy.

This trial has merit due to its randomised nature and acknowledgement of other factors which may affect retinopathy, including age, sex and duration of diabetes. However, there is no description given as to what adjustment was made. Furthermore, although the article claims to investigate 1,170 patients, they were actually only screened; 327 patients were further investigated by qualified retinal photographers. It is also likely that patients with poor thyroid health would be more susceptible to poor health and lifestyle in general. It is this author's opinion that more needs to be known about this relationship. Hypothyroidism has not yet been established as a definitive risk factor.

Pregnancy

Gestational diabetes (diabetes occurring in pregnancy) should be highlighted when giving advice to patients who are, or wish to become pregnant. If patients are considered at risk they should be closely monitored. Gestational diabetes usually occurs in the second or third trimester, and often ceases after the birth. The strain on the body to produce extra insulin in this period may cause the mother-to-be to become prematurely diabetic; poor control of existing diabetes can

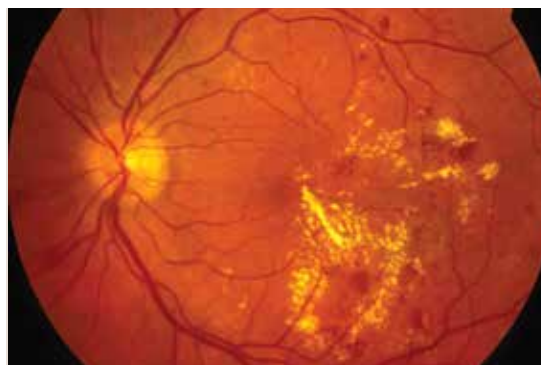


Figure 2 Diabetic maculopathy is a major cause of sight loss in the UK



exacerbate problems during pregnancy.

If a diabetic woman is pregnant, this poses a threat to her unborn baby, and every effort should be made to tighten the mother's diabetic control. Babies of diabetic women have a three-fold risk of death in the first few months of life.⁹ Furthermore, while the condition is related to the period of pregnancy, those who develop gestational diabetes are more at risk of long-term complications: the lifetime risk of developing Type 2 diabetes after gestational diabetes is 30 per cent.

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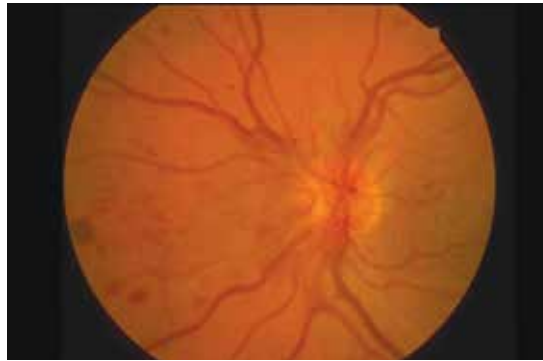


Figure 3 Proliferative retinopathy (here shown as new vessels at the disc) is related to poor systemic control of the disease

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● Michelle Sarah Barry is a pre-registration optometrist

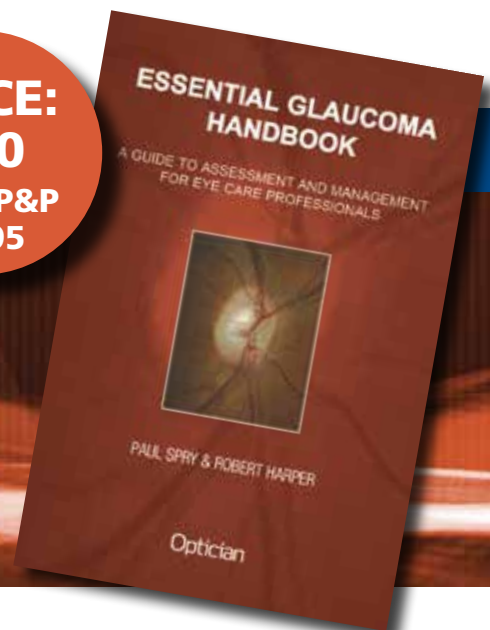
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