Prevalence of diabetic retinopathy in children and adolescents with type-1 diabetes attending summer camps in France


APHP, Ophthalmology Department, Lariboisière Hospital, Paris 7 University, 2, rue Ambroise Paré, 75475 Paris, France

Institut inter régional pour la santé (IRSA), Tours, France

Association “Aide aux Jeunes Diabétiques” (Aid to Young Diabetics-AJD), France

APHP, Department of Endocrinology, Diabetes and Metabolic Diseases, hôpital Avicenne, Bobigny, France

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Abstract

Objective. – To evaluate, using fundus photography, the prevalence of diabetic retinopathy (DR) in young diabetic subjects attending summer camps run by the Aide aux Jeunes Diabétiques Association (Aid to Young Diabetics).

Research design and methods. – Five hundred and four children and adolescents (250 boys and 254 girls), with type 1 diabetes mellitus, aged 10–18 years (mean: 13 ± 2), were screened for DR using non mydriatic photography, during their stay in a holiday camp. Demographic and clinical data recorded on subjects’ arrival in the camp included date of birth, height, weight, treatment, blood pressure, and duration of diabetes. HbA1c was determined with a DCA 2000 kit.

Results. – Mean diabetes duration was 4.8 ± 3.4 years and mean HbA1c was 8.5 ± 1.3%. Mild non proliferative DR was diagnosed in 23 children (4.6%). Compared to subjects without DR, those with DR were significantly older (P < 10^-3), had a longer duration of diabetes (P = 0.001), higher systolic blood pressure (P = 0.04), and had higher (but not significantly so) HbA1c (P = 0.15). After adjustment for age, only longer duration remained significantly associated with DR (P = 0.01).

Conclusion. – The prevalence of DR in these young patients was low compared to that reported in previous studies. The decrease may be due to modern diabetes care with multiple insulin injections. However, early detection of DR in adolescents, especially in their late teens, remains important, because it allows the identification of patients at high risk of progression towards severe stages of DR.

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Résumé

Prévalence de la rétinopathie diabétique chez des enfants et des adolescents atteints de diabète de type 1

But. – Évaluer la prévalence de la rétinopathie diabétique (RD) à l’aide de photographies du fond d’œil, chez de jeunes patients diabétiques fréquentant les camps de vacances de l’association « Aide aux jeunes diabétiques » (AJD).

Matériel et méthodes. – Un dépistage de la RD par photographies du fond d’œil a été réalisé chez 504 enfants et adolescents (250 garçons et 254 filles), diabétiques de type 1 âgés de 10 à 18 ans (moyenne: 13 ± 2) pendant leur séjour en camp de vacances. Les données démographiques et cliniques recueillies à l’arrivée dans le camp sont les suivantes : date de naissance, poids, taille, traitement, tension artérielle, durée du diabète. L’HbA1c a été déterminée grâce à un kit DCA 2000.

Résultats. – La durée moyenne du diabète était de 4,8 ± 3,4 ans et l’HbA1c, moyenne de 8,5 ± 1,3 %. Une RD non proliférante minime a été trouvée chez 23 enfants (4,6 %). Les sujets qui avaient une RD étaient significativement plus âgés (P < 10^-3), avaient une durée plus longue de diabète (P = 0,001), une pression artérielle systolique plus élevée (P = 0,04), et tendaient à avoir une HbA1c plus élevée (P = 0,15) que les sujets sans RD. Après ajustement sur l’âge, seule la durée plus longue du diabète était significativement associée à la présence d’une RD (P = 0,01).

* Corresponding author.
E-mail address: p.massin@lrb.aphp.fr (P. Massin).

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1. Introduction

The prevalence of diabetic retinopathy (DR) in young diabetic children is low, but events during the teenage years may greatly increase the risk of developing microvascular complications [1,2]. Current guidelines recommend annual screening for all diabetic patients, starting at age 10 [3–5]. The prevalence of DR in young children and adolescents varies from 10% to 35%, depending on the different studies, but few data are available for France [6–11]. The aim of this study was to evaluate, using non mydriatic fundus photography, the prevalence of DR in a group of diabetic children and adolescents attending summer camps run by the Aide aux Jeunes Diabétiques Association (AJD).

2. Patients and methods

The AJD is a place where physicians and non physicians use original tightly-organized structures to help diabetic children and their families to improve their treatment and live normally. Every year, the association organizes summer camps for young diabetic subjects where they can enjoy sports and fun activities in a medical environment. This allows them to acquire vital information relating to their therapeutic education, such as understanding their condition, the possible occurrence of complications, including retinopathy, as well as the importance of early diagnosis of these complications. The cost of stays at AJD summer camps is entirely covered by the French healthcare system. More than 1000 medical/educational stays (1200) are organized every year during school holidays. Our study was conducted in five AJD summer camps in the south of France, and covered 10 1–3-week periods during July and August 2004. Patients and their parents gave informed consent for their complication assessment.

The demographic and clinical data recorded on the children’s arrival in the camp were date of birth, height, weight, treatment, blood pressure, and duration of diabetes. HbA1c was determined with a DCA 2000 kit (Bayer Diagnostics, Puteaux, France) in 6 min, with the NGSP/DCCT immunoturbidimetric method, from one drop of capillary blood obtained via a finger stick. The quality of the kit was checked before use in each new camp.

Prepubertal age was arbitrarily defined as 0–12 years in males, and 0–11 in females.

Screening for DR was performed using fundus photography with a non mydriatic camera, by a mobile unit traveling from camp to camp. The non mydriatic camera was an NW6-TRC Topcon camera (Topcon Europe, Rotterdam, The Netherlands), connected to a digital camera (Fuji, S2-PRO, Fuji, Tokyo, Japan). Images were captured in true color (24 bits) at a resolution of 1490 × 960 pixels, resulting in an image size of 4MB. Five 45° non stereoscopic images of five overlapping fields were taken for each eye: one image was centered on the macula, including the optic disc, and one each were centered on the nasal, temporal, upper and lower fields. This allowed coverage of a total view angle of about 120 degrees. With this non mydriatic camera, retinal photographs were taken without pupil dilation in a well-darkened room by an orthop- tist. Images were stored on a CD ROM, and sent for grading to the Ophthalmology Department of the Lariboisière Hospital, where they were graded twice by two independent ophthalmologists (A.E. and P.M.).

The quality of each photograph was scored on the following 4-grade scale: grade1: excellent, grade 2: definition limited, difficult to assess, grade 3: only gross detail visible, and grade 4: not gradable.

DR was classified according to the ALFEDIAM classification, a modified version of the ETDRS classification [4], using the following five grades of severity: no DR; early DR, with retinal hemorrhage or soft exudates but no microaneurysms; mild non proliferative DR: microaneurysms only; moderate non proliferative DR: with moderate intraretinal hemorrhages, soft exudates, and occasional intraretinal microvascular anomalies; severe non proliferative DR: with numerous peripheral retinal hemorrhages and/or moderate intraretinal microvascular anomalies and/or definite venous beadings; and proliferative DR: with newvessels on the disc or elsewhere on the retina. Macular edema was diagnosed from the presence of hard exudates within one disc diameter of the foveola.

2.1. Statistical methods

Results were expressed as means ± standard deviations, and percentages with 95% confidence intervals (95% CI). Qualitative data were compared in subjects with and without retinopathy using the chi² test, and quantitative data were compared in these groups using the ANOVA general linear model, with age as a covariate. The prevalence of DR before and after the start of puberty was compared by Fisher’s exact test. The significance level was set at < 5%. The software used was Version 2000 of the Number Cruncher Statistical Systems (NCSS, Dr Hintze, Kaysville, UT, USA).
3. Results

Five hundred and four young diabetic subjects (254 girls and 250 boys) with type 1 diabetes were screened for DR. Their mean age was 13.2 ± 1.9 years. Diabetes onset was prepubertal in 443 (88%) and postpubertal in 61 (12%). The mean duration of diabetes was 4.9 ± 3.5 years (Fig. 1). The mean HbA1c measured during the subjects’ stay in the summer camp was 8.5 ± 1.3% (Nl: 5 ± 0.35%), and in 151 (30%) it was below 8%. The mean daily dose of insulin was 0.92 U/kg. Eighty-six subjects (17%) had two injections of insulin per day, 136 (27%) had three or four, and 267 (52.9%), more than four; 16 (3.1%) used continuous subcutaneous insulin infusion via a portable minipump.

The quality of the fundus photographs, taken without pupil dilation, was excellent in all cases, and allowed the detection and grading of DR under good conditions. Agreement between the grading of the two ophthalmologists was excellent. They only disagreed in four cases, which they graded jointly in order to reach a consensus.

Twenty-three of the 504 young diabetic subjects (13 girls and 10 boys) had DR (4.6%). Their mean age was 15.5 ± 1.65 (range, 11–17). Nine of them had early DR (retinal hemorrhage or soft exudates, without microaneurysms) and 14, 15.5 ± 1.65 (range, 11–17), mild DR. One young girl, aged 17, had small retinal macular hemorrhage or soft exudates, without microaneurysms) and 14, 15.5 ± 1.65 (range, 11 – 17). Nine of them had early DR (retinal hemorrhage or soft exudates, without microaneurysms) and 14, 15.5 ± 1.65 (range, 11–17), mild DR. One young girl, aged 17, had small retinal macular hemorrhage or soft exudates, without microaneurysms) and 14, 15.5 ± 1.65 (range, 11–17), mild DR. One young girl, aged 17, had small retinal macular hemorrhage or soft exudates, without microaneurysms) and 14, 15.5 ± 1.65 (range, 11–17), mild DR. One young girl, aged 17, had small retinal macular hemorrhage or soft exudates, without microaneurysms) and 14, 15.5 ± 1.65 (range, 11–17), mild DR. One young girl, aged 17, had small retinal macular hemorrhage or soft exudates, without microaneurysms) and 14, 15.5 ± 1.65 (range, 11–17), mild DR. One young girl, aged 17, had small retinal macular hemorrhage or soft exudates, without microaneurysms) and 14.

The prevalence of DR increased exponentially with age (Fig. 2a): it was 1% from 10 to 13 years, 5.8% from 14 to 15, and 7.7% from 16 to 18. It also rose exponentially with the duration of diabetes (Fig. 2b) and with the increase in HbA1c (Fig. 2c).

After adjustment for age, only longer duration of diabetes remained significantly associated with DR (P = 0.01). The clinical characteristics of the young patients according to age at diabetes onset are given in Table 2. Despite a significantly shorter diabetes duration in the post-puberty onset group, the prevalence of DR was not significantly different in the pre- and post-puberty onset groups, while mean HbA1c was significantly higher in post-puberty onset group (P < 10⁻³).

### Table 1

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>No DR</th>
<th>DR</th>
<th>P</th>
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<tbody>
<tr>
<td>N</td>
<td>481</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Males (%)</td>
<td>49.9</td>
<td>43.5</td>
<td>0.55</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.1 (1.8)</td>
<td>15.0 (1.7)</td>
<td>0.0000001</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>20.0 (3.1)</td>
<td>21.2 (2.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>109 (11)</td>
<td>114 (13)</td>
<td>0.04</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>67 (10)</td>
<td>71 (9)</td>
<td>0.09</td>
</tr>
<tr>
<td>Prepubertal diabetes onset (%)</td>
<td>87.9 (84.7–90.7)</td>
<td>87.0 (66.4–97.2)</td>
<td>0.89</td>
</tr>
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</table>

### Table 2

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Before puberty</th>
<th>After puberty</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>13.0 ± 1.8 years</td>
<td>14.8 ± 1.5 years</td>
<td>&lt;10⁻³</td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>5.3 ± 3.4 years</td>
<td>1.4 ± 1.1 years</td>
<td>&lt;10⁻³</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.6 ± 1.3</td>
<td>7.9 ± 1.6</td>
<td>&lt;10⁻³</td>
</tr>
<tr>
<td>Prevalence of DR (%)</td>
<td>20 (4.5%)</td>
<td>3 (4.9%)</td>
<td>0.75</td>
</tr>
</tbody>
</table>

*Kruskal–Wallis or chi² test.

4. Discussion

In this study, we found that the overall prevalence of DR in a group of young diabetic patients attending summer camps in France was 4.6%. This prevalence is low compared to that reported in previously published studies [6–15], which ranged from 10% to 50%. The difference may be due to several factors, including the methods used to screen for DR, the type of population screened, the age of the patients, and the duration of diabetes.

Several methods can be used to screen for DR: the most sensitive is mydriatic stereoscopic fundus photography, which has been shown to be as sensitive as fluorescein angiography for detecting early signs of DR [16]. Non mydriatic non stereo-
scopic fundus photography, now currently used to screen for DR, is highly sensitive to screen for DR compared to the standard reference method of mydriatic stereoscopic photography, and is especially effective in young patients [17–20]. Indeed, with non mydriatic photography, image quality depends largely on pupil size, and this type of photography has limitations in older patients because they have smaller pupils [18,20]. In our patients, all fundus photographs were of very good quality and gradable. The low prevalence of DR was therefore not due to a lack of sensitivity of the screening method used.

DR prevalence is usually lower in community-based populations like the group studied here, than in hospital-based populations. According to previous reports on French children with type 1 diabetes, the present sample of young diabetic patients constitutes about 5.2% of the total number of children and adolescents with type 1 diabetes in the 10–19-year age group [21]. There are indeed around 10–15,000 children and adolescents with diabetes in France. Our group seems representative of the overall population of young diabetic subjects, as they came from different backgrounds, their main motivation for attending an AID summer camp was to meet other young diabetics and share their experience as well as sports and playful activities. This group does not seem to represent a sample of “motivated” young diabetic patients with better glycemic control, which could have explained the low DR prevalence we found, because their mean HbA1c was very similar to the mean HbA1c reported by the Joslin Clinic in 300 children in 2001, by Bouhanick in a sample of young diabetic subjects in France in 2003, and by Maguire et al. in their most recent series [15,22,23].

Of the many risk factors considered, longer duration of diabetes and poorer glycaemic control have repeatedly been reported as independent risk factors for DR in children and adolescents [6,9,10,12,13]. Compared to previous series, our patients were younger and had shorter diabetes duration, which may explain their lower DR prevalence. Indeed, 217 of them (43%) had had diabetes for less than 4 years (Fig. 1). However, among 194 young diabetic patients with a median age and duration of diabetes almost the same as in our group, Falck et al. [9] still found a DR prevalence of 10.8%, i.e. higher than ours. Our diabetic population’s mean HbA1c was 8.5 ± 1.3%, which is lower than the mean HbA1c that Rosilio et al. [21] reported in a cross-sectional nationwide study of 2579 French children with type 1 diabetes in 1995, and also much lower than the mean HbA1c of the adolescents in the DCCT control group, which was 9.76% [24]. In addition, 30% of our young patients had an HbA1c below 8%. This improved glycemic control compared to that of the DCCT control group may therefore have contributed to the low DR prevalence we found.

The DCCT and the Epidemiology of Diabetes Interventions and Complications (EDIC) studies have indeed clearly and unambiguously demonstrated that in adolescents, intensive diabetes therapy delays the onset of the disease and slows the progression of microvascular complications, including DR, in adolescents [24–27]. Furthermore, the DR prevalence reported in recent studies is lower than in earlier investigations: thus, Kernell et al. [8] reported a 14.5% prevalence of DR in 557 young diabetic subjects whose mean age was 14.6 years, and Scott et al. [11], a 13% prevalence in a group of 251 young diabetic patients aged less than 26, compared to a prevalence ranging from 34% to 45% in studies published between 1985 and 1995 [6,7,12,14]. In addition, Maguire et al. [15] found an overall prevalence of 42% for DR in adolescents with type 1 diabetes screened between 1989 and 1992, and a lower prevalence of 20.3% in a subsequent series followed between 1990 and 2002. Nordwall et al., as well as Lecaire et al. [28,29] also reported a declining incidence of both severe retinopathy and nephropathy in patients with type 1 diabetes diagnosed in childhood, due to modern diabetes care with multiple insulin injections, and treatment by ACE inhibitors. Finally, in a recent paper, Kong et al. [30] reported a very low 0.7%-prevalence of

Fig. 2. Prevalence of DR.

a. According to age.
b. According to diabetes duration.
c. According to HbA1c.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Diabetic retinopathy (%)</th>
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<tbody>
<tr>
<td>10–11</td>
<td>1.0% (n=66)</td>
</tr>
<tr>
<td>12–13</td>
<td>1.0% (n=192)</td>
</tr>
<tr>
<td>14–15</td>
<td>5.8% (n=154)</td>
</tr>
<tr>
<td>16–18</td>
<td>17.7% (n=62)</td>
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<table>
<thead>
<tr>
<th>Diabetes duration (years)</th>
<th>Diabetic retinopathy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 (n=239)</td>
<td>2.1%</td>
</tr>
<tr>
<td>5–10 (n=226)</td>
<td>6.2%</td>
</tr>
<tr>
<td>&gt;10 (n=39)</td>
<td>13.0%</td>
</tr>
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<table>
<thead>
<tr>
<th>HbA1c (%)</th>
<th>Diabetic retinopathy (%)</th>
</tr>
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<tbody>
<tr>
<td>&lt;7.6 (n=114)</td>
<td>3.5%</td>
</tr>
<tr>
<td>7.6–8.4 (n=141)</td>
<td>3.5%</td>
</tr>
<tr>
<td>8.5–9.4 (n=142)</td>
<td>4.9%</td>
</tr>
<tr>
<td>9.5–10.4 (n=69)</td>
<td>5.8%</td>
</tr>
<tr>
<td>&gt;10.4 (n=38)</td>
<td>7.9%</td>
</tr>
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</table>
DR in a group of 382 young diabetic patients whose mean age was 15.8 years.

The decrease in DR prevalence reported in recent studies was observed despite a persistently high mean HbA1c, which was higher than the HbA1c recommended by the DCCT [24, 25]. However, most young diabetic patients are now treated with either multiple injections or insulin pumps, and in our study, only 86 of them (17.5%), had two injections of insulin per day. Therefore, as suggested by Maguire et al. [15], and Moshin et al. [31] the lower prevalence of DR observed in most recent studies may be partly due to fewer glucose excursions.

The presence of DR in our series was associated with older age, longer diabetes duration, higher BMI, higher HbA1c, and higher systolic blood pressure. These are the risk factors usually associated with DR [6–13]. Only one of the children under 12 had DR, and its prevalence increased with age, reaching 17.7% in adolescents aged 16 or more. In all cases, DR was mild. This is in agreement with most previous reports [9, 15,24]. Severe DR is rare before the age of 17, and severe forms in adolescents were only reported in one recent study, in two children aged 12 and 13, respectively, who had severe NPDR [8].

The role of puberty and the contribution of the duration of prepubertal diabetes to the development of DR have been controversial. It was suggested that the duration of diabetes during the years preceding puberty may not affect the development of microvascular complications [32–34]. However, although most authors reported that puberty had a relatively protective effect, prepubertal diabetes duration was found to be an independent risk factor for the development of DR [35–38]. The period, however, contributes less compared to the years after puberty. Donaghue et al. [35] found that the increment for clinical retinopathy was 28% for each year of prepubertal duration, compared to 36% for each year of post pubertal duration. This may be due to hormonal changes, including increased growth hormone and insulin-like growth factor-1 levels, and to worse glycemic control after puberty [35,39,40]. In most of the children in our study, diabetes onset occurred before puberty. However, despite shorter diabetes duration in those with onset after puberty, DR prevalence did not differ in this group from that of the group with onset before puberty; this finding is therefore consistent with previous reports that the years before puberty do not contribute much to the development of DR.

Despite the apparently decreasing prevalence of DR in children and adolescents, its detection is still important, because the presence of mild DR may be a risk factor for progression towards more severe forms. This may not apply to young children, in whom mild DR may regress spontaneously, according to Maguire et al.’s [15] findings. However, spontaneous improvement of DR is less likely to occur in older children and adolescents. Lastly, the presence of mild DR in groups of young diabetic patients at higher risk, whose HbA1c exceeds 10% and whose diabetes duration is longer than 10 years, should be an indicator for more frequent retinal screening [15]. Indeed, this higher risk group may develop an extremely severe form of DR called florid DR, which may progress within a few months to sight-threatening DR and loss of vision, especially in the late teens [41,42]. In addition, the DCCT and EDIC study results suggest that the risk of DR progression is higher in adolescents than in older-onset type 1 diabetic subjects [24–27]; thus, the cumulative incidences of a progression of 3 steps or more in the ETDRS retinopathy level, from DCCT baseline to EDIC Year 4, were 65% and 32%, respectively, in the conventional and intensive groups of the original adolescent cohorts, compared to 49% and 18%, respectively, for the entire cohort of type 1 diabetic subjects. This may be due in part to globally worse glycaemic control in the original adolescent cohort than in older type 1 diabetic subjects during both the DCCT and EDIC studies, but still underlines the higher risk of DR progression in these young patients.

In conclusion, our results suggest that the prevalence of DR in diabetic children and adolescents is declining, although the long-term outcome of childhood-onset type 1 diabetes remains more severe than that of adult-onset diabetes [1,10]. This strengthens the need for more frequent screening for complications, including DR. Non mydriatic fundus photography seems particularly suitable for DR screening in young patients, because the absence of pupillary dilation, combined with the rapidity of the screening procedure, are both advantages that may increase the compliance of these patients with the recommended annual fundus examination.

Acknowledgments

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