BMJ Open Diabetes Research & Care

Socioeconomic deprivation and development of diabetic retinopathy in patients with type 1 diabetes mellitus

Pablo Alvarez-Ramos,[1] Soledad Jimenez-Carmona,[1,2,3] Pedro Alemany-Marquez,[1,2,3] Juan Antonio Cordoba-Doña,[3,4] Manuel Aguilar-Diosdado [3,5]

To cite: Alvarez-Ramos P, Jimenez-Carmona S, Alemany-Marquez P, *et al*. Socioeconomic deprivation and development of diabetic retinopathy in patients with type 1 diabetes mellitus. *BMJ Open Diab Res Care* 2020;**8**:e001387. doi:10.1136/bmjdrc-2020-001387

Received 20 March 2020
Revised 24 August 2020
Accepted 5 September 2020

[1]Ophtalmology Department, Hospital Universitario Puerta del Mar, Cadiz, Spain
[2]Surgery Department, Universidad de Cádiz Facultad de Medicina, Cadiz, Spain
[3]Research Institute of Biomedicine of Cadiz (INiBICA), Cadiz, Spain
[4]Public Health Department, Hospital Universitario de Jerez de la Frontera, Jerez de la Frontera, Spain
[5]Endocrinology and Nutrition Department, Hospital Universitario Puerta del Mar, Universidad de Cadiz, Cadiz, Spain

Correspondence to
Dr Manuel Aguilar-Diosdado; manuel.aguilar.sspa@juntadeandalucia.es

ABSTRACT

Introduction Very little is known about the influence of socioeconomic status on type 1 diabetes mellitus (T1DM) complications. Our aim was to determine whether socioeconomic level is a risk factor for the development of diabetic retinopathy (DR) in patients with T1DM.

Research design and methods A cohort of 150 patients with T1DM were studied prospectively over 9 years. Socioeconomic status was assessed using a neighborhood-level measure based on an index of deprivation. The contribution of other variables such as hypertension, dyslipidemia, diabetic nephropathy and smoking habit was evaluated. Cox proportional hazards models were used to quantify the associations.

Results The incidence of DR was 21.6 cases per 1000 patient-years. Multivariable analyses showed that for each percentage point increase in glycated hemoglobin (HbA1c), the risk of developing DR increased by 58% (HR 1.58, 95% CI 1.19 to 2.10).

Patients with T1DM onset >18 years of age and resident in areas of lower socioeconomic levels presented with almost triple the risk of developing DR (HR 2.95, 95% CI 1.08 to 8.00) compared with those with onset <18 years of age and resident in less deprived areas. We did not find significant relationships with other variables studied such as hypertension, dyslipidemia, diabetic nephropathy and smoking habit.

Conclusions Low socioeconomic level is a risk factor, independent of glycemic control, in the development of DR in patients with T1DM when the onset of diabetes is in adulthood. This finding indicates that socioeconomic status and age of onset need to be considered in population screening for DR in patients with T1DM.

Significance of this study

What is already known about this subject?

- Although socioeconomic status is related to important chronic diseases in general and type 2 diabetes mellitus in particular, very little is known about its influence on complications in patients with type 1 diabetes mellitus.

What are the new findings?

- In our study we observed a clear association between the level of socioeconomic deprivation and the incidence of diabetic retinopathy, independent of the level of the patient's glycemic control.

How might these results change the focus of research or clinical practice?

- It is essential to develop and promote new social policies centered in patients with type 1 diabetes mellitus with the objective of reducing the consequences of social inequalities in groups with low socioeconomic levels.

INTRODUCTION

Diabetes mellitus (DM) comprises several clinical entities with different etiologies, but which has hyperglycemia as its principal characteristic.[1] The worldwide prevalence of DM in 2017 was estimated at around 425 million persons, and this level is expected to rise by 48% by 2045 to reach a level of 629 million.[2] Of the total number of patients with DM, approximately 5%–10% suffer type 1 diabetes mellitus (T1DM) (1 in every 300–500 people <18 years of age).

Diabetic retinopathy (DR) is the principal cause of acquired blindness in developed countries, and represents 5% of all causes of acquired blindness worldwide. One in every three patients with DM have some grade of DR, and is three times more prevalent in patients with T1DM than with type 2 diabetes mellitus (T2DM).[3] The duration of the disease and metabolic (glycemic) control have been traditionally considered the principal risk factors associated with the appearance and progression of DR in patients with DM. Other factors such as hypertension, dyslipidemia, diabetic nephropathy, and the smoking habit have been described as having some involvement as well.[3–6]

Socioeconomic factors influencing the development and progression of some clinical processes have been well documented, such as in cardiovascular diseases.[7 8] In DM, data indicate that a low socioeconomic level is associated

with a poorer clinical evolution of the complications specific to DM, such as higher morbidity and mortality,[9 10] even in countries with universal healthcare systems.

A low socioeconomic status has been associated with delayed diagnosis and poorer outcomes in cases of amblyopia,[11] macular edema[12] and glaucoma.[13 14] Low economic status has also been associated with higher DR prevalence and more advanced forms of the disease. This has been attributed to lower participation in screening programs,[15–17] as well as lower likelihood of being routinely followed up.

The principal objective of our study was to analyze the relationship between socioeconomic level and the development of DR in a cohort of patients with T1DM, without DR at the start of the follow-up. Other influencing factors taken into account were the level of metabolic control, hypertension, dyslipidemia, diabetic nephropathy, and the smoking habit.

This project was implemented in southern Spain (Andalusia) within the context of a universal public health service. The comprehensive program ('Integrated Plan for Diabetes in Andalusia') includes early detection of DR using digital retinography.[18 19]

RESEARCH DESIGN AND METHODS

Study ambit

The study was developed within the catchment area of the *Hospital Universitario Puerta del Mar de Cádiz* (Andalusia, Spain) which provides healthcare for 247 000 citizens, of whom approximately 1500 are patients with T1DM.

Study design

The prospective cohort of patients with T1DM belonged to the Early Diabetic Retinopathy Detection Plan (*Plan de Detección Precoz de la Retinopatía Diabética*) of Andalusia conducted using digital imaging or retinography, and with a maximum period of follow-up of 9 years.

Study subjects

A total of 150 patients with T1DM, without DR at the start of the follow-up, were recruited into the study. Of these, 78 had early-onset (0–18 years of age) T1DM, and 72 at a later age (>18 years).[20] The duration of the follow-up of the cohort was for 9 years, between 2008 and 2017.

DM diagnosis was performed according to American Diabetes Association guideline.[21] When the patients had equivocal signs and symptoms of T1DM (such as ketoacidosis) at the start of the study, diagnosis was confirmed by the presence of autoantibodies (antiglutamic decarboxylase and anti-IA2) and decrease in fasting C-peptide (<0.5 ng/dL) and fasting plasma glucose >250 mg/dL or following intravenous glucagon-stimulated C-peptide test.[22]

Inclusion criteria

Patients with T1DM >14 years of age, without DR at the start of the follow-up and who are within the catchment area of the *Puerta del Mar University Hospital* (Cádiz).

Exclusion criteria

Retinography with signs of other ocular disease, or non-evaluable retinography, or type of DM other than T1DM.

Variables recorded in the study

Dependent variables

Grade of DR: Defined and classified according to the International Clinical Diabetic Retinopathy Disease Severity Scale. In case of different grades of severity in the two eyes, we accepted the eye with the greater severity as reference.

Duration of the T1DM: Numbers of years between the age of onset of the T1DM and the age when the retinography first showed signs of DR. For patients not developing DR, the duration was considered up to the last retinography performed in the follow-up.

Independent variables

Age at onset of T1DM: Data collected from the electronically stored patient history.

Grade of metabolic control: Determined as the level of glycated hemoglobin (HbA1c) (mmol/L and %). For the statistical analyses we used the baseline HbA1c and mean HbA1c obtained from the annual determinations recorded during the follow-up.

Arterial hypertension: Dichotomous variable. The patient was considered to be hypertensive if this was recorded (>140/90 mm Hg) at DM diagnosis, or patients receiving any antihypertension medication.

Dyslipidemia: Dichotomous variable. Defined as the presence of high low-density lipoprotein cholesterol (LDL cholesterol >100 mg/dL) and/or hypertriglyceridemia (triglycerides >200 mg/dL)[23] or patients being in receipt of hypolipidemic medication, recorded at DM diagnosis.

Diabetic nephropathy: Dichotomous variable. Defined as the presence of renal damage by direct method (renal biopsy), albumin excretion ≥30 mg/g creatinine (urinary albumin/creatinine ratio) or ≥30 mg/24 hours confirmed in at least two or three samples in the previous 6 months, or glomerular filtration of <60 mL/min/1.73 m^2, calculated with the Cockcroft-Gault equation for conventional (24-hour urine) creatinine clearance, or isotopic methods.

Smoking habit: Dichotomous variable. Defined by current consumption, or consumption in the year prior to the start of the follow-up period.

Socioeconomic status: To measure the socioeconomic status of the cases, an artificial index of deprivation of the census tract of residence was used. The index has been applied previously in epidemiological research on inequalities in mortality and morbidity in Andalusia.[24 25]

The index is calculated for each census tract using three census variables: (1) the percentage of persons (both genders) with low levels of education (unable to read or write, or <5 years of conventional schooling) in the general population ≥16 years of age; (2) the percentage of unemployed people (unemployed population ≥16

years divided by the actively employed population ≥16 years); and (3) the percentage of unskilled workers (unskilled population ≥16 years divided by the employed population ≥16 years). A principal component analysis was carried out with the standardized values of the three variables to calculate the index. The necessary conditions for its application were verified by the Bartlett sphericity test and the Kaiser-Meyer-Olkin sampling adequacy measure. The census tracts were ranked and categorized into five groups according to quintiles. Level 1 represents the areas with the least deprivation and level 5 represents the sectors with the highest levels of deprivation in the population.

Follow-up

Annually, from the date of inclusion in the study, three images of each eye were made with a non-mydriatic digital retinography (Topcon NW-200). One of the images centered in the macula (central), another in the optic disc (nasal) and another temporal to the macula (temporal). All images were reviewed independently by two DR expert ophthalmologists (authors SJC, PAM).

The first retinography free of DR was considered as the basal level. The detection of any grade of DR requiring ophthalmological treatment, or other alterations that required specialist evaluation, signaled the transfer of the patient out of the follow-up study.

Statistical analyses

The baseline characteristics of the patients included in the study were established and the cumulative incidence and the incidence rate of DR were calculated. Person-years of follow-up were estimated for each case by computing the time between the date of onset and the date of last follow-up, with respect to the development of DR or the completion of the study. The risk factors associated with the development of DR were compared. Initially, the distributions of these factors between those patients who did develop DR were compared with those who did not develop DR using χ^2 test for categorical variables and the Mann-Whitney U test for quantitative variables. The incidence rates of subgroups of each of the risk factors were calculated, as were the incidence rate ratios with their 95% CIs. Finally, once the most important covariables were identified, regression models were developed using Cox proportional hazards models to calculate the adjusted HR of each of the variables, using years from diagnosis of T1DM up to the event as the time variable. In the final step, interaction between the included variables was tested and added to the model in case they yielded statistical significance.

RESULTS

Demographic variables

The baseline characteristics of the patients are presented in table 1. Of the total patients in the screening program, 150 (78/150 women) without DR were incorporated in the follow-up program. The mean age at the start of the study was 31.6±11.6 years, with a mean age at onset of T1DM of 19.9±11.3 years, and a mean duration of DM of 17±8.9 years of clinical evolution of DM at the start of the follow-up period. The mean HbA1c was 7.7% (60 mmol/mol), and 68.7% of the patients had HbA1c >7% (53 mmol/mol). Hypertension was present in 15.3%, dyslipidemia in 16.7%, diabetic nephropathy in 6.7% and smoking habit in 24.7%. Nearly 16% of the patients (n=23) were resident in socioeconomic-deprived (grades 4 and 5) census tracts (table 1).

Table 1 Baseline characteristics of the patients at the start of the study (n=150)

Parameter	DR not developed (n=95)	DR developed (n=55)
Age (years)	31.9±11.8	31±11.2
Sex (%) (males:females)	47.4/52.6	49.1/50.9
Age at onset (years)	22.3±10.5	15.7±11.5
Duration of T1DM (years)	9.7±7.2	15.4±9.5
HbA1c (%)	7.6±1.3	7.8±1.1
HbA1c >7% (%)	63.2	78.2
Hypertension (%)	15.8	14.5
Dyslipidemia (%)	13.7	21.8
Diabetic nephropathy (%)	6.3	7.3
Smoking habit (%)	25.3	23.6
Deprivation index (level 1), n (%)	42 (44.2)	17 (30.9)
Deprivation index (level 2), n (%)	34 (27.8)	19 (34.5)
Deprivation index (level 3), n (%)	6 (6.3)	9 (16.4)
Deprivation index (level 4), n (%)	11 (11.6)	6 (10.9)
Deprivation index (level 5), n (%)	2 (2.1)	4 (7.3)

DR, diabetic retinopathy; HbA1c, glycated hemoglobin; T1DM, type 1 diabetes mellitus.

Cumulative incidence and incidence rate of DR

At the end of the follow-up period, of the 150 patients studied (2250 patient-years), 55 had presented with DR, implying a cumulative incidence of 36.6% and an incidence rate of 21.6/1000 patient-years. Of these 55 patients with DR, 30 were slight and 25 were of moderate DR, implying an incidence of 20.0% and 16.6%, respectively. We did not observe any severe case of DR at the end of the follow-up period.

Risk factors associated with DR development

Table 2 summarizes the principal characteristics studied in patients who developed DR, as well as those who did not develop DR over the long-term follow-up. In the bivariate analysis, we observed that the patients with DR were younger at the onset of T1DM (15.7±11.5 vs 22.3±10.5

Table 2 Distribution of vascular disease risk factors in the population studied

Variable	DR not developed (n=95)	DR developed (n=55)	P value
Age (years)	31.9±11.8	31±11.2	0.590
Males (%)	47.4	49.1	0.830
Age of DM onset (years)	22.3±10.5	15.7±11.5	0.001
Age of onset >18 years (%)	61	38.1	0.007
Duration of T1DM (years)	9.7±7.2	15.4±9.5	0.001
HbA1c baseline (%)	7.6±1.3	7.8±1.1	0.040
HbA1c mean (%)	7.6±1.1	7.8±1.1	0.060
HbA1c >7% (%)	63.2	78.2	0.050
Hypertension (%)	15.8	14.5	0.830
Dyslipidemia (%)	13.7	21.8	0.190
Diabetic nephropathy (%)	6.3	7.3	0.820
Smoking habit (%)	25.3	23.6	0.820

DM, diabetes mellitus; DR, diabetic retinopathy; HbA1c, glycated hemoglobin; T1DM, diabetes mellitus.

years; p<0.050), had a longer duration of the disease (15.4±9.5 vs 9.7±7.2 years; p<0.050), higher values of basal HbA1c (7.8%±1.1% (62 mmol/mol) vs 7.6%±1.3% (59 mmol/mol); p<0.05) and mean HbA1c (7.8%±1.1% (62 mmol/mol) vs 7.6%±1.1% (60 mmol/mol); p=0.060) over the period of follow-up.

Table 3 summarizes the incidence rate for each socioeconomic category, and the incidence rate ratio of DR of the different variables studied. The patients with HbA1c >7% had an incidence rate of 24.0 cases/1000 patient-years, while the rate was 14.7 cases/1000 patient-years in those with HbA1c <7% (p=0.078). With respect to the socioeconomic variable, the DR incidence rate in those with levels 4 and 5 (higher deprivation) compared with those with levels 1–3 (less deprivation) was 25.7 cases/1000 patient-years vs 21.4 cases/1000 patient-years; p=0.291.

The results obtained with the Cox proportional hazards regression (table 4) showed that, in the final model, the variables that explained the most risk of developing DR were: HbA1c, age of onset of DM, and level of deprivation associated with the residence census tract. The proportional hazards model indicates that these three variables have independent influences on the log hazard function describing the risk of DR.

Following adjustment for covariates in the model, HbA1c was significantly associated with developing DR (hazard rate: 1.6; 95% CI 1.19 to 2.10), that is, for every point increase in the mean value of HbA1c there is an increase of 60% in risk of DR. Also, the adjusted model identified a significant interaction between the level of deprivation and the age of onset of DM. Compared with the reference level (onset of DM <18 years of age and resident in less socioeconomically deprived area), the group with later onset (>18 years of age) and resident in the area of highest socioeconomic deprivation had triple the risk of developing DR (HR 2.95; 95% CI 1.08 to 8.00). No significant associations of the appearance of DR were observed with the rest of the combinations of age of onset and socioeconomic status.

Additionally, to rule out a potential role of HbA1c in mediating the effect of socioeconomic status on the development of DR, we calculated the mean and SD of HbA1c in each of the six subgroups; very similar results were observed (onset <18 years and less deprived=7.94±1.16; onset <18 years and medium deprivation=7.74±0.98; onset <18 years and deprived=7.98±1.47; onset >18 years and less deprived=7.40±0.61; onset >18 years and medium deprivation=7.63±1.42; onset >18 years and deprived=7.85±1.10).

DISCUSSION AND CONCLUSIONS

In our study we observed a clear association between the level of socioeconomic deprivation and the incidence of DR, independent of the level of the patient's glycemic control. This relationship is evident when the results are

Table 3 Incidence rate and the incidence rate ratio of DR

Variable	Cases: person-years	Incidence rate (×1000 person-years)	Incidence rate ratio	95% CI	P value
Sex (male/female)	28:1370/27:1180	20.4/22.8	0.9	0.51 to 1.57	0.338
Deprivation; census section (4–5/1–3)	10:389/45:2107	25.7/21.4	1.2	0.5 to 2.4	0.291
HbA1c (>7%/<7%)	45:1873/10:677	24/14.7	1.6	0.80 to 3.61	0.078
Onset (>18/≤18 years)	21:1194/34:1356	17.5/25	0.7	0.38 to 1.24	0.101
Hypertension (yes/no)	8:481/47:2069	16.6/22.7	0.7	0.29 to 1.56	0.213
Dyslipidemia (yes/no)	12:546/43:2004	21.9/21.4	1.1	0.49 to 1.97	0.459
Diabetic nephropathy (yes/no)	4:168/51:2382	23.8/21.4	1.1	0.29 to 3.02	0.394
Smoking habit (yes/no)	13:585/42:1965	22.2/21.3	1.1	0.51 to 1.97	0.441

DR, diabetic retinopathy; HbA1c, glycated hemoglobin.

Table 4 Cox proportional hazards model for the development of DR in patients with T1DM

Variable	Category	HR	95% CI	P value
HbA1c mean (%)		1.6	1.19 to 2.10	0.002
Age of onset of DM Deprivation: census section	<18 years/no deprivation	Reference	–	–
	<18 years/medium deprivation	1	0.44 to 2.49	0.986
	<18 years/high deprivation	0.5	0.20 to 1.46	0.227
	≥18 years/no deprivation	0.7	0.24 to 1.88	0.454
	≥18 years/medium deprivation	1.2	0.51 to 2.96	0.640
	≥18 years/high deprivation	2.9	1.08 to 8.00	0.033
Sex	Male	Reference	–	–
	Female	0.9	0.48 to 1.60	0.694

DM, diabetes mellitus; DR, diabetic retinopathy; HbA1c, glycated hemoglobin; T1DM, type 1 diabetes mellitus.

analyzed as a function of onset of DM. That is, patients who had an onset at >18 years of age and from a lower socioeconomic area present with an almost tripled level of risk of developing DR than those who developed DM in infancy or adolescence and from areas of less deprivation. However, in the rest of the combinations of age of onset and socioeconomic levels, we did not find any significant associations.

The finding of an association between low socioeconomic level and the development of DR concurs with other studies published to date by various research groups, and in different geographic areas. The relationship between education level and the development of DR was described by Klein *et al*[26] who observed a higher risk of DR in women with a low education level, coexisting with early onset of DM. Two subsequent studies conducted in the UK also described associations between low education level and a high prevalence of DR.[27 28] Our results are similar to those obtained in a study conducted in China in which a higher education level and higher net income were associated with reduced DR incidence.[29]

A study conducted in France analyzed the correlation between the index of individual deprivation ('EPICES scores') and glycemic control with the associated complications of DM. The authors found that the prevalence of DR was higher in patients with lower socioeconomic level (mean 3.66; 95% CI 1.39 to 9.64; p=0.009) and that this association persisted following adjustment for glycemic control.[30] Several studies in the UK correlated low socioeconomic level with DR. One of these studies observed an association between low socioeconomic level (measured as the 'Index of Multiple Deprivation') and the presence of DR susceptible to treatment.[15] Another study showed similar outcome for T1DM[17] but no significant association for T2DM, and another showed the presence of this association with proliferative DR.[16] Such associations detected were shown to be independent of the duration of the disease, the values of HbA1c, the concentrations of lipoproteins, and presence of hypertension.

Only in the study published by Klein *et al*[26] was there a difference observed between the onset of DM and the influence of socioeconomic factors in the development of DR. In this case, a greater risk was observed in patients with onset <18 years of age, which is contrary to that observed in our study in which the risk is increased in those patients who had onset >18 years of age.

Several hypotheses have been proposed to explain the relationship between socioeconomic deprivation and the increased risk of DR. Different factors have been invoked such as poor access to healthcare services because of the existence of economic barriers, or even factors associated with a clear deterioration of the quality of life. One postulation is that environmental factors in deprived areas can unlink immune responses in individuals genetically predisposed to developing T1DM, which can accelerate the appearance, or progression, of complications of the disease.[31] Another postulation is that of a lower participation in primary prevention screening programs in more deprived areas[15] which could increase the risk of more advanced forms of DR being identified in later diagnosis. Further, it is important to consider the impact of the complications of DM on the education level and working practices, especially when DR complications are involved. In our case, the high healthcare cover in the population (especially pediatric services) could explain the lower influence of socioeconomic status of the patients with early onset. The education level could be another factor explaining the interaction between onset of DM and the socioeconomic level since there would not be as much influence in the pediatric population, as there may be in adulthood, that is, in our universal healthcare system, the neonates are followed up with more attention than subsequent adolescence or adulthood when the uptake of healthcare facilities is more a function of the individual's choice.

We observed an incidence rate of 21.6 cases/1000 patient-years and a cumulative incidence of various grades of DR of 36.6%. To the best of our knowledge, there has been only one study of incidence density of DR in cohorts of patients with T1DM. The study had observed 97.7 cases/1000 person-years.[32] This is a finding that is much higher than ours. In the UK, disparate cumulative incidences between 47% and 97% have been published by Wisconsin Epidemiologic Study of Diabetic

Retinopathy.[33–36] Other studies, as well, have observed incidence levels much lower than ours, of between 20% and 35%.[37–39] To compare these studies we must take into account two fundamental factors jointly: the duration of the T1DM at the start of the follow-up, and the grade of glycemic control. DR is time dependent and several studies show that with a sufficiently long follow-up time, most patients with T1DM will develop DR, so that the time of evolution of DM can be considered the main risk factor for DR.[36 40]

The other fundamental factor influencing the incidence of DR is glycemic control. Patients with poor metabolic control present with higher incidences[33 34 41] than those with better control.[37 42] In our cohort of patients, those who developed DR presented with a higher baseline HbA1c than those who did not develop DR, and in multivariable analyses, the mean HbA1c levels were shown to be an independent risk factor for the development of DR; with no significant differences noted with respect to sex. These data are concordant with those published in other studies that showed HR between 1.2[37]and 4.2.[43]

We did not observe any significant association in the development of DR with respect to the other risk factors such as hypertension, dyslipidemia, diabetic nephropathy, and the smoking habit. In similar studies, an association was observed between hypertension and DR especially between diastolic pressure and proliferative DR.[35 41] With respect to dyslipidemia, Romero-Aroca *et al* observed significant association between the ApoB/ApoA1 ratio and the LDL to high-density lipoprotein cholesterol ratio and DR.[40 42] Similarly, significant associations between DR and diabetic nephropathy[6] and smoking[44] have been communicated. This disparity in the findings could be due to several causes including the heterogeneity of the study sample, and the duration of DM follow-up. The population studied was characterized by its youth, as well as the absence, almost, of comorbidities.

Of importance is our novel finding that there is a significant relationship between economic deprivation and incidence of DR in patients with T1DM. Our results suggest that socioeconomic levels need to be taken into account as a risk factor when designing screening strategies for DR. Also, this factor affects the adherence to outpatient clinic consultations and screening programs; especially in those individuals who were diagnosed with T1DM after 18 years of age. As such, it is essential to develop and promote new social policies centered on this risk group with the objective of reducing the consequences of social inequalities in groups with low socioeconomic levels. Despite there being universal healthcare provision in our environment with free access to healthcare, the socioeconomic level still appears to play a significant role.

As limitations of the study, we need to highlight that the results obtained refer to a specific hospital catchment area and, as such, is not translatable to other situations with different characteristics. Also, comparisons with other studies need to be undertaken with caution because of the different measures of socioeconomic status. Moreover, our study requires further specific details on variables associated with service utilization, for example, the number of visits or adherence to treatment which may associate with socioeconomic status and, as such, could shed more light on the links between deprivation and DR.

Hence, we consider it necessary to apply this study model to other studies under different socioeconomic conditions in order to confirm the impact of the socioeconomic deprivation, together with other risk factors of known importance, in the development of DR in patients with T1DM.

Acknowledgements We thank all the patients and healthcare professionals who participated in this protracted project. Editorial assistance was by Dr Peter R Turner.

Contributors SJC, JACD, and MAD designed the study. PAR, SJC and PAM collected the data. PAR, SJC, PAM, JACD and MAD interpreted the data. PAR, JACD and MAD drafted the manuscript. All authors have read and approved the final version of the manuscript. PAR and MAD take responsibility for the integrity of the data, and for submitting the manuscript for publication.

Funding The study was funded by the Instituto de Salud Carlos III (grant number: PI11/02924) and by the Andalusia Ministry of Health ITI-FEDER (grant number: PI-0029-2017).

Competing interests None declared.

Patient consent for publication Obtained.

Ethics approval This study was approved by the Ethics Committee of the Puerta del Mar University Hospital (ID: 80/2011).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The deidentified data have been obtained from digital medical records (demographic, clinical and analytical variables); the assessment of the socioeconomic status was assessed using a neighborhood-level measure based on an index of deprivation. Data are available to BMJ held by the authors.

ORCID iD

Manuel Aguilar-Diosdado http://orcid.org/0000-0001-9657-5949

REFERENCES

1 American Diabetes Association. *Standards of Medical Care in Diabetes-2017* Abridged for Primary Care Providers. *Clin Diabetes* 2017;35:5–26.
2 International Diabetes Federation (IDF). *IDF diabetes atlas*. 7th edition, 2015.
3 Yau JWY, Rogers SL, Kawasaki R, *et al*. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care* 2012;35:556–64.
4 The Diabetes Control and Complications Trial Research Group. Progression of retinopathy with intensive versus conventional treatment in the diabetes control and complications trial. diabetes control and complications trial Research Group. *Ophthalmology* 1995;102:647–61.
5 Stratton IM, Kohner EM, Aldington SJ, *et al*. UKPDS 50: risk factors for incidence and progression of retinopathy in type II diabetes over 6 years from diagnosis. *Diabetologia* 2001;44:156–63.
6 Hammes HP, Kerner W, Hofer S, *et al*. Diabetic retinopathy in type 1 diabetes-a contemporary analysis of 8,784 patients. *Diabetologia* 2011;54:1977–84.
7 Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation* 1993;88:1973–98.
8 Colhoun HM, Hemingway H, Poulter NR. Socio-Economic status and blood pressure: an overview analysis. *J Hum Hypertens* 1998;12:91–110.

9 Espelt A, Borrell C, Roskam AJ, *et al*. Socioeconomic inequalities in diabetes mellitus across Europe at the beginning of the 21st century. *Diabetologia* 2008;51:1971–9.
10 Scott A, Chambers D, Goyder E, *et al*. Socioeconomic inequalities in mortality, morbidity and diabetes management for adults with type 1 diabetes: a systematic review. *PLoS One* 2017;12:e0177210.
11 Smith LK, Thompson JR, Woodruff G, *et al*. Social deprivation and age at presentation in amblyopia. *J Public Health Med* 1994;16:348–51.
12 Sharma HE, Mathewson PA, Lane M, *et al*. The role of social deprivation in severe neovascular age-related macular degeneration. *Br J Ophthalmol* 2014;98:1625–8.
13 Fraser S, Bunce C, Wormald R, *et al*. Deprivation and late presentation of glaucoma: case-control study. *BMJ* 2001;322:639–43.
14 Nessim M, Denniston AK, Nolan W, *et al*. Research into glaucoma and ethnicity (ReGAE) 8: is there a relationship between social deprivation and acute primary angle closure? *Br J Ophthalmol* 2010;94:1304–6.
15 Scanlon PH, Carter SC, Foy C, *et al*. Diabetic retinopathy and socioeconomic deprivation in Gloucestershire. *J Med Screen* 2008;15:118–21.
16 Lane M, Mathewson PA, Sharma HE, *et al*. Social deprivation as a risk factor for late presentation of proliferative diabetic retinopathy. *Clin Ophthalmol* 2015;9:347–52.
17 Low L, Law JP, Hodson J, *et al*. Impact of socioeconomic deprivation on the development of diabetic retinopathy: a population-based, cross-sectional and longitudinal study over 12 years. *BMJ Open* 2015;5:e007290.
18 Aguilar-Diosdado M, Amo M, Lama C, *et al*. Ii plan integral de diabetes de Andalucía 2009-2013. ED: Junta de Andalucía. *Consejería de Salud* 2009:1–137.
19 Aguilar-Diosdado M, Mayoral E, Regife V, *et al*. Early detection of diabetic retinopathy using ocular fundus digital imaging : The Andalusia Diabetic Retinopathy Detection Program. *Diabetes* 2015;64:2448.
20 Thomas NJ, Lynam AL, Hill AV, *et al*. Type 1 diabetes defined by severe insulin deficiency occurs after 30 years of age and is commonly treated as type 2 diabetes. *Diabetologia* 2019;62:1167–72.
21 American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2014;37 Suppl 1:S81–90.
22 Bonser AM, Garcia-Webb P. C-Peptide measurement and its clinical usefulness: a review. *Ann Clin Biochem* 1981;18:200–6.
23 American Diabetes Association. Standards of medical care in diabetes--2014. *Diabetes Care* 2014;37 Suppl 1:S14–80.
24 Ruiz-Ramos M, Escolar Pujolar A, Sánchez Perea J, *et al*. Trends in social inequalities in mortality in the city of Seville [Spain] (1994-2002). *Gac Sanit* 2006;28:89–96.
25 Córdoba-Doña JA, Novalbos-Ruiz JP, Suárez-Farfante J, *et al*. Social inequalities in HIV-TB and non-HIV-TB patients in two urban areas in southern Spain: multilevel analysis. *Int J Tuberc Lung Dis* 2012;16:342–7.
26 Klein R, Klein BE, Jensen SC, *et al*. The relation of socioeconomic factors to the incidence of proliferative diabetic retinopathy and loss of vision. *Ophthalmology* 1994;101:68–76.
27 Chaturvedi N, Stephenson JM, Fuller JH. The relationship between socioeconomic status and diabetes control and complications in the EURODIAB IDDM complications study. *Diabetes Care* 1996;19:423–30.
28 Bachmann MO, Eachus J, Hopper CD, *et al*. Socio-Economic inequalities in diabetes complications, control, attitudes and health service use: a cross-sectional study. *Diabet Med* 2003;20:921–9.
29 Tao X, Li J, Zhu X, *et al*. Association between socioeconomic status and metabolic control and diabetes complications: a cross-sectional nationwide study in Chinese adults with type 2 diabetes mellitus. *Cardiovasc Diabetol* 2016;15:61.
30 Bihan H, Laurent S, Sass C, *et al*. Association among individual deprivation, glycemic control, and diabetes complications: the EPICES score. *Diabetes Care* 2005;28:2680–5.
31 Atkinson MA, Eisenbarth GS, Michels AW, *et al*. Type 1 diabetes. *Lancet* 2014;383:69–82.
32 Ou H-T, Lee T-Y, Li C-Y, *et al*. Incidence of diabetes-related complications in Chinese patients with type 1 diabetes: a population-based longitudinal cohort study in Taiwan. *BMJ Open* 2017;7:e015117.
33 Klein R, Klein BE, Moss SE, *et al*. The Wisconsin epidemiologic study of diabetic retinopathy. X. four-year incidence and progression of diabetic retinopathy when age at diagnosis is 30 years or more. *Arch Ophthalmol* 1989;107:244–9.
34 Klein R, Klein B, Moss S. The Wisconsin epidemiologic study of diabetic retinopathy. *Arch Ophthal* 1994;112:1217–28.
35 Klein R, Klein BE, Moss SE, *et al*. The Wisconsin epidemiologic study of diabetic retinopathy: XVII. The 14-year incidence and progression of diabetic retinopathy and associated risk factors in type 1 diabetes. *Ophthalmology* 1998;105:1801–15.
36 Klein R, Knudtson MD, Lee KE, *et al*. The Wisconsin epidemiologic study of diabetic retinopathy: XXII the twenty-five-year progression of retinopathy in persons with type 1 diabetes. *Ophthalmology* 2008;115:1859–68.
37 Wang SY, Andrews CA, Herman WH, *et al*. Incidence and risk factors for developing diabetic retinopathy among youths with type 1 or type 2 diabetes throughout the United States. *Ophthalmology* 2017;124:424–30.
38 Wang N-K, Lai C-C, Wang J-P, *et al*. Risk factors associated with the development of retinopathy 10 yr after the diagnosis of juvenile-onset type 1 diabetes in Taiwan: a cohort study from the CGJDES. *Pediatr Diabetes* 2016;17:407–16.
39 Martín-Merino E, Fortuny J, Rivero-Ferrer E, *et al*. Incidence of retinal complications in a cohort of newly diagnosed diabetic patients. *PLoS One* 2014;9:e100283.
40 Romero-Aroca P, Baget-Bernaldiz M, Reyes-Torres J, *et al*. Relationship between diabetic retinopathy, microalbuminuria and overt nephropathy, and twenty-year incidence follow-up of a sample of type 1 diabetic patients. *J Diabetes Complications* 2012;26:506–12.
41 Broe R, Rasmussen ML, Frydkjaer-Olsen U, *et al*. The 16-year incidence, progression and regression of diabetic retinopathy in a young population-based Danish cohort with type 1 diabetes mellitus: the Danish cohort of pediatric diabetes 1987 (DCPD1987). *Acta Diabetol* 2014;51:413–20.
42 Romero-Aroca P, Baget-Bernaldiz M, Fernandez-Ballart J, *et al*. Ten-Year incidence of diabetic retinopathy and macular edema. risk factors in a sample of people with type 1 diabetes. *Diabetes Res Clin Pract* 2011;94:126–32.
43 Romero-Aroca P, Navarro-Gil R, Valls-Mateu A, *et al*. Differences in incidence of diabetic retinopathy between type 1 and 2 diabetes mellitus: a nine-year follow-up study. *Br J Ophthalmol* 2017;101:1346–51.
44 Uruska A, Araszkiewicz A, Uruski P, *et al*. Higher risk of microvascular complications in smokers with type 1 diabetes despite intensive insulin therapy. *Microvasc Res* 2014;92:79–84.