

Clinical and Psychological Course of Diabetes From Adolescence to Young Adulthood

A longitudinal cohort study

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OBJECTIVE — To determine the clinical and psychological course of diabetes through adolescence and the relationship with glycemic control in young adulthood.

RESEARCH DESIGN AND METHODS — A longitudinal cohort study of adolescents recruited from the register of the outpatient pediatric diabetes clinic. A total of 76 individuals (43 male patients, 33 female patients) aged 11–18 years completed baseline assessments, and 65 individuals (86%) were reinterviewed as young adults (20–28 years of age). Longitudinal assessments were made of glycemic control (HbA_{1c}), weight gain (BMI), and development of complications. Adolescents completed self-report questionnaires to assess emotional and behavioral problems as well as self-esteem. As young adults, psychological state was assessed by the Revised Clinical Interview Schedule and the self-report Brief Symptom Inventory.

RESULTS — Mean HbA_{1c} levels peaked in late adolescence and were worse in female participants (average 11.1% at 18–19 years of age). The proportion of individuals who were overweight (BMI >25.0 kg/m²) increased during the 8-year period from 21 to 54% in female patients and from 2 to 28% in male patients. Serious diabetes-related events included death in one patient and cognitive impairment in two patients. Individuals in whom diabetic complications developed (25% of male patients and 38% of female patients) had significantly higher mean HbA_{1c} levels than those without complications (difference 1.9%, 95% CI 1.1–2.7, $P < 0.0001$). Behavioral problems at baseline were related to higher mean HbA_{1c} during the subsequent 8 years ($\beta = 0.15$, SEM (β) 0.04, $P < 0.001$, 95% CI 0.07–0.24).

CONCLUSIONS — The outcome for this cohort was generally poor. Behavioral problems in adolescence seem to be important in influencing later glycemic control.

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Adolescence is a difficult time for people with type 1 diabetes because glycemic control often deteriorates (1) and the risk of developing long-term complications seems to accelerate (2). The role of hyperglycemia in the development of microvascular complica-

tions has been demonstrated conclusively by the results of the Diabetes Control and Complications Trial (3). It has been argued that poor control in adolescence relates to the physiological changes of puberty (4); however, problems of adherence to treatment regimens (5) and atten-

dance at outpatient visits (6) suggest that psychological factors are also important.

Psychiatric disorders have been shown to be more common in both adolescents and young adults with type 1 diabetes than in nondiabetic populations (7,8). However, the influence of psychological state in adolescence on later diabetic outcomes has not been established; the three previous longitudinal cohort studies in adolescents were based on younger children and comprised small numbers of participants or selective samples (9–11).

We used a prospective longitudinal design in a representative population of teenagers to determine the clinical and psychological course of diabetes from adolescence to young adulthood and the relationship between psychological state in adolescence and later diabetes outcomes.

RESEARCH DESIGN AND METHODS

Subjects

The index group of adolescents were identified through the case register of the pediatric outpatient clinic at the John Radcliffe Hospital, Oxford, U.K. The clinic provides specialist treatment by a multidisciplinary team of doctors, nurses, dieticians, and a child psychologist. It is the only clinic serving children and adolescents with type 1 diabetes within the catchment area of John Radcliffe Hospital, and almost all children with type 1 diabetes in this area are known to the clinic, whether or not they attend regularly. If patients were experiencing problems, they were encouraged to attend the clinic more frequently. In 1989, 86 patients aged 11–18 years who had been diagnosed with diabetes more than 1 year prior were identified. Of these, 76 patients (88%) agreed to participate in a study of psychological well-being and eating habits (12). In 1997, these patients were approached again and reinterviewed

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

to determine their progress. Most patients were still attending clinics in Oxford; others were traced through general practitioners or the computerized records of the district health authority health service. Clinical notes were audited in 69 patients (91%), and 65 patients (85%) agreed to a second interview and assessment.

Of the patients who were not reinterviewed at follow-up, two had died; one died from diabetic ketoacidosis and the other died from a cause unrelated to diabetes. One patient developed cognitive impairment from hypoglycemia, and another patient was excluded from the follow-up assessment because of a concurrent illness that would have confounded his responses to the interview. Three patients refused to participate, three patients could not be traced, and one physician declined to give permission to contact a patient with a known psychiatric disorder.

Measures

Baseline assessment (1989–1990).

Adolescent psychological state was assessed using Achenbach and Edelbrock's Youth Self Report and Profile, a well-validated scale that yields two summary scales: an "internalizing scale" relating to emotional problems, including symptoms of anxiety and depression, and an "externalizing scale" relating to behavioral problems of aggressive antisocial conduct (13). Self-esteem was assessed using the Coopersmith Inventory (14). In addition, parents completed the Child Behavior Checklist, which is the parents' corresponding version of the Youth Self Report (15). Height, weight, and HbA_{1c} were measured. Eating habits and attitudes were also assessed, and these results have been reported previously (12,16).

Follow-up assessment (1997–1998).

Most patients were attending the specialist diabetes young-adult clinic. Informed consent was obtained, and patients were invited for a second interview with the research nurse. Assessments of psychological symptoms were made using the self-report Brief Symptom Inventory (17,18), which measures severity of mood and other symptoms (the Global Severity Index gives a continuous score of increasing symptoms), and the Revised Clinical Interview Schedule (19), a research diagnostic interview that yields categorical diagnoses. Height, weight, and blood pressure were measured, and

Table 1—Characteristics of the study cohort

	Baseline		Follow-up	
	Male patients	Female patients	Male patients	Female patients
<i>n</i>	43	33	39	26
Age (years)	15.2 ± 2.2	15.3 ± 1.9	23.7 ± 2.1	23.9 ± 2.0
Duration of diabetes	8.0 ± 3.7	7.1 ± 2.9	16.3 ± 3.5	15.7 ± 2.9
HbA _{1c}	9.4 ± 2.5	9.7 ± 1.8	9.6 ± 1.8	9.3 ± 1.9
BMI	20.1 ± 2.4	22.7 ± 3.7	24.0 ± 2.5	24.7 ± 2.6
BMI SDS*	0.21 ± 0.85	0.77 ± 0.75†	0.29 ± 0.86‡	0.79 ± 0.75§
Complications			(<i>n</i> = 40)	(<i>n</i> = 29)
Severe retinopathy	0	0	1	2
Nephropathy	0	0	6	5
Multiple	0	0	1	3
Hypertension	0	0	2	1

Data are means ± (SD). *Cohort BMI standard deviation score (SDS) vs. normal population data, †*P* < 0.001, ‡*P* < 0.05. Severe retinopathy = laser-treated proliferative retinopathy only, nephropathy = microalbuminuria or proteinuria only, multiple = both severe retinopathy and nephropathy, hypertension = antihypertensive therapy (with no nephropathy).

details of social characteristics, smoking, alcohol consumption, and diabetes management were recorded. A capillary blood sample was obtained for measurement of HbA_{1c}, and three consecutive early morning or overnight urine specimens were collected for measurement of urinary creatinine:albumin ratio. The Central Oxford Research Ethics Committee approved the study.

Case note review. Medical notes were reviewed after completion of the follow-up assessment to ensure blinding of the research nurse. Details recorded included clinic attendance, serial measurements of HbA_{1c} (minimum 4 years for each patient, average 20–25 results per patient), and documented laser-treated proliferative retinopathy and/or incipient nephropathy. Prescription of antihypertensive medication was noted, and referrals for psychiatric assessment during the follow-up period were recorded.

Assay

From 1987 to 1991, HbA₁ was measured by a Glytrac electroendosmosis method (Ciba Corning Diagnostics, Halstead, U.K.). From 1991 and thereafter, HbA_{1c} was measured by high-performance liquid chromatography (normal range 4.3–6.1%) using a Biorad Diamat automated glycosylated hemoglobin analyzer (Biorad Laboratories, Hemel Hempstead, Hertfordshire, U.K.) (20). The changeover between the two methods was carefully documented, and appropriate regression

equations were available for conversion of the earlier data to the current method, which is documented in detail elsewhere (2).

Albumin was measured by double-antibody enzyme-linked immunosorbent assay (2). Creatinine was measured using the modified Jaffe method (Unimate 7) on a Cobas Mira automated spectrophotometer (Roche Diagnostic Systems, Basel, Switzerland). Details of interassay and intra-assay variability of the glycated hemoglobin assays and of the albumin and creatinine assays are documented elsewhere, along with the definitions of incipient nephropathy (microalbuminuria) (2).

Statistical methods

Parametric data were analyzed using Student's *t* test, nonparametric data were analyzed using Mann-Whitney *U* test, and categorical data were analyzed with Fisher's exact test. BMI was calculated (kg/m²), and the standard deviation score was derived from published standards (21,22).

Multiple and logistic regression analyses were performed to examine the potential role of psychological factors and self-esteem on the following outcomes: mean HbA_{1c} during the 8-year follow-up period, psychological state at follow-up, and admission for diabetic ketoacidosis. The following variables were entered as independent variables: gender, behavioral (externalizing) subscale, emotional (internalizing) subscale, self-esteem (all

from baseline), and baseline HbA_{1c} (as an index of diabetes control).

RESULTS — Characteristics of the patients participating in each assessment are shown in Table 1. There was no difference between the mean age or duration of diabetes in patients who participated in the initial study at baseline and patients who were not interviewed or between patients who completed both interviews and patients who were interviewed only at baseline.

General outcomes

Clinic attendance. Average frequency of clinic attendance for patients at baseline was 3.6 visits per year (minimum 2 visits, maximum 8 visits). Average frequency of clinic attendance for patients in the year before the follow-up assessment was 2.2 visits (minimum 0 visits, maximum 7 visits). At follow-up, six patients (9%) were still attending the pediatric clinic, 33 patients (51%) were attending the specialist young adult diabetic clinic for patients aged 17–25 years, and the remaining patients were cared for by the adult clinic, a clinic outside the region, or a general practitioner. Two patients (3%) had not attended any clinic appointments in the 12 months before follow-up.

Social characteristics. At follow-up, five male patients (13%) and 14 female patients (54%) were married. None of the patients were unemployed; by comparison, the rates of unemployment for age-/sex-matched strata in the general U.K. population ranged from 4–13% (23). A total of 47 patients (72%) had undertaken further education after 16 years of age, including 17 patients (26%) taking degree courses. This proportion was similar to data for the general U.K. population (23).

Smoking and alcohol consumption. At follow-up, 14 male patients (36%) and one female patient (4%) were regular smokers (10 cigarettes or more per day), and 11 male patients (28%) and 1 female patient (4%) routinely consumed more than 21 and 14 units of alcohol per week, respectively.

Diabetes management. The number of patients on multiple-injection regimens increased from 36 patients (47%) at baseline to 52 patients (80%) at follow-up. There was no significant difference in HbA_{1c} at either assessment between patients on multiple-injection regimens and those who received injections twice daily.

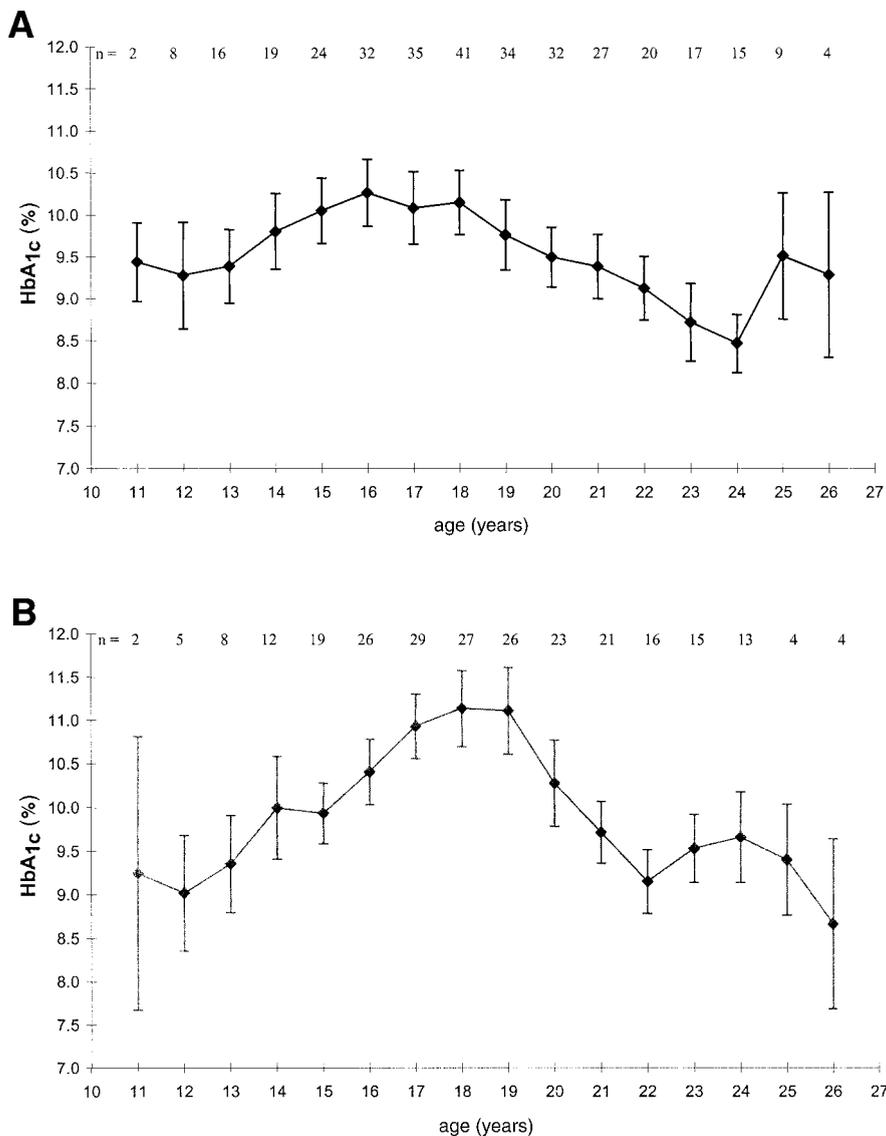


Figure 1—Mean HbA_{1c} (and SEM [bars]) for male patients (A) and female patients (B) by age.

Median home blood glucose testing at both assessments was 28 times per month (baseline interquartile range 12–56 tests per month, follow-up interquartile range 5–76 tests per month).

Glycemic control. There was no difference in the mean HbA_{1c} between baseline and follow-up (Table 1), although longitudinal data showed that mean HbA_{1c} was highest during late adolescence (Fig. 1A and B). Individual HbA_{1c} data demonstrated that glycemic control had improved in 31 patients (46%) between assessments and deteriorated in 37 patients (54%). The patients in whom HbA_{1c} improved between assessments were significantly older than those in whom HbA_{1c} deteriorated (24.4 [1.8] vs.

23.2 years [2.0], difference 1.2, 95% CI 0.3–2.2, *P* < 0.01). In the patients >22 years of age at follow-up, mean HbA_{1c} decreased from 18 to 22 years of age by 1.4% for the male patients and 2.8% for the female patients (the mean HbA_{1c} at 18 years of age was comparable to the mean HbA_{1c} from the whole cohort).

Weight. Female patients were significantly overweight at both assessments, and male patients were significantly overweight at follow-up only (Table 1). The number of female patients with a BMI >25.0 kg/m² increased from 7 (21%) at baseline to 14 (54%) at follow-up. The number of male patients with a BMI >25.0 kg/m² increased from 1 (2%) initially to 11 (28%) at follow-up.

Serious events. During the 8-year follow-up (622 person-years exposure), serious events occurred in three patients (4%) as a result of diabetes. One male patient died at 19 years of age during his 11th episode of diabetic ketoacidosis in a 3-year period. Another male patient had undergone long-term rehabilitation after an episode of cerebral edema that developed during diabetic ketoacidosis at 14 years of age. In total, two male patients (5%) and eight female patients (26%) were admitted with recurrent diabetic ketoacidosis (defined as two or more admissions during the study period). One female patient was cognitively impaired after an episode of severe hypoglycemia due to an insulin overdose. Other serious events, unrelated to diabetes, were the death of one female patient and development of schizophrenia in another female patient shortly after the initial interview.

Complications. At baseline, none of the patients had diabetic complications. By follow-up, 10 male patients (25%) and 11 female patients (38%) had serious microvascular complications or required treatment for hypertension (Table 1). Mean HbA_{1c} level during the 8-year study period was significantly higher in patients with complications (11.3 [1.4] vs. 9.4% [1.7], difference 1.9%, 95% CI 1.1–2.7, $P < 0.0001$); the occurrence of frequent admissions for diabetic ketoacidosis was also higher in patients with complications (24 vs. 4%, difference 20%, 95% CI 0.6–39, $P < 0.02$). Duration of diabetes was not related to the presence of complications.

Psychological outcomes

At baseline, female patients had more emotional symptoms than male patients (difference 8.0, 95% CI 3.0–13.0, $P < 0.001$) and lower self-esteem (difference –8.41, 95% CI –16.0 to –0.61, $P < 0.03$). There was an association between the total scores of the children's self-report and the parents' report (Spearman's $r_s = 0.40$, $P < 0.001$).

At follow-up, seven female patients (27%) and three male patients (8%) scored as suffering from a psychiatric disorder on the Clinical Interview Schedule. During the study period, psychiatric referrals had been sought for four male patients (10%) and seven female patients (23%); reasons were varied and included assessment for repeated time out of school, treatment for an eating disorder, and depression. In three female patients

Table 2—Multiple regression analysis with mean HbA_{1c} level as a dependent variable

Independent variables	β	SEM (β)	t	95% CI of β
Sex	0.81	0.53	1.53	–0.25 to 1.87
Baseline behavioral state	0.15	0.04	3.61*	0.07 to 0.24
Baseline emotional state	0.06	0.03	1.96†	–0.002 to 0.13
Baseline self-esteem	0.004	0.02	0.17	–0.04 to 0.05

* $P < 0.001$; † $P < 0.06$.

in whom follow-up interviews were not possible, extensive psychiatric care was required. Reasons included recurrent insulin or tablet overdoses, self-harm, and mismanagement of diabetes; inpatient treatment for schizophrenia was required in one patient.

Psychological predictors

In multivariate analysis, adolescent behavioral problems were significantly related to higher mean HbA_{1c} during the subsequent 8 years (Table 2). A trend also showed an association between adolescent emotional problems and lower mean HbA_{1c} level. Although self-esteem was associated with concurrent psychological adjustment (Spearman's $r_s = 0.59$, $P < 0.0001$), when entered into the model, it was not a significant predictor of mean HbA_{1c}, indicating that self-esteem did not act as a mediating factor. Recurrent hospital admission for diabetic ketoacidosis was the only significant predictor of psychological state at follow-up, as measured by the Global Severity Index ($t = 4.4$, $P < 0.001$, 95% CI 0.4–1.1). None of the baseline variables were related to recurrent hospital admissions for diabetic ketoacidosis.

CONCLUSIONS— This study is the first to examine in detail the clinical and psychological course of diabetes from adolescence to young adulthood, and the generally poor outcome for this longitudinal cohort has important implications for routine clinical care. Among the patients in our study, we found educational qualifications comparable to those of the general population and no unemployment. However, we also found regular smoking and excess alcohol consumption, a relatively high mean HbA_{1c} level, a problem of weight gain, a number of serious adverse events, and a high rate of diabetic complications. Multivariate analysis showed associations between baseline psychological problems and mean glycaemic control over the follow-up period and

between recurrent hospital admissions for diabetic ketoacidosis and current psychological state. An advantage of the study was that it was based on a general clinic population from a representative district. We are confident that almost all patients within this geographically defined area were identified at baseline. A limitation of the study was the relatively small sample size, and the failure to reinterview some of the patients with very poor outcomes may have underestimated the morbidity experienced by this cohort.

General outcomes

As a direct consequence of diabetes, one patient died and two patients became cognitively impaired. In addition, one other patient died, one female patient developed schizophrenia after a history of drug abuse and poor diabetes control, and one female patient with multiple diabetic complications was too psychologically disturbed to be reinterviewed. The number of these serious events is of great concern and is consistent with a recent study that demonstrated this as a high-risk age group (24). Although there are few comparable available data, one other adolescent longitudinal cohort study of a similar size also reported two deaths (25).

Despite the overall failure to achieve good glycaemic control, especially in female patients, longitudinal HbA_{1c} data did improve with age. Although the mean HbA_{1c} level was still relatively poor at follow-up, this was probably due to the proportion of patients in late adolescence, when HbA_{1c} levels were highest. This peak at 18–19 years of age is later than might have been expected. Since the baseline study, multiple-injection regimens have become normal practice and appropriate adjustments are now made for insulin requirements during puberty (4). However, the effect this changing pattern of care has had on glycaemic control is unclear. Although HbA_{1c} levels in the Oxford clinics have decreased over the years,

in the ongoing Oxford Regional Prospective Study of Childhood Diabetes, which provides comparable longitudinal HbA_{1c} data over a wider geographical area, the recently reported mean HbA_{1c} level from 468 children was similar to this earlier cohort at 9.9% (1.7) (2).

Psychological outcomes

Adolescent behavioral problems of aggression and antisocial conduct were adversely associated with poorer glycemic control (HbA_{1c}) during adolescence and young adulthood. Interestingly, there was a trend for emotional problems, such as anxiety and depression, to be associated with lower glycemic control. This association was found in a previous study, which suggested that anxious children may be more diligent in monitoring and may take more effective action in response to signs of poor blood glucose control (26). Low self-esteem was also associated with poor glycemic control, but this did not seem to mediate the relation between psychological problems and poor outcome. The high prevalence of psychiatric morbidity at follow-up in our young adults is comparable to our previous study of young adults, which reported higher psychiatric morbidity in patients with diabetes compared with the general population (8). Referral for psychiatric assessment was common and was most often observed in those patients who also had recurrent hospital admissions for diabetic ketoacidosis. The only predictor of the Global Severity Index of mental state at follow-up was recurrent hospital admissions for diabetic ketoacidosis, suggesting that when diabetes is significantly out of control, it raises the risk of psychological morbidity.

Implications of the study

This longitudinal cohort study demonstrated a poor outcome in a significant proportion of young adults with diabetes, despite intensive individualized care and support by the diabetes team and, when required, psychiatric and psychological referrals. Identification of psychological and behavioral problems at a young age will require targeting more effective intervention for at-risk patients, if the significant morbidity associated with diabetes during the transition from childhood to young adulthood is to be reduced.

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