Psychosocial Factors and Complications of IDDM

The Pittsburgh Epidemiology of Diabetes Complications Study. VIII.

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OBJECTIVE— To investigate whether psychosocial factors are associated with diabetic complications.

RESEARCH DESIGN AND METHODS— Questionnaires on quality of life, depressive symptomatology, and personality type were completed and a clinical assessment was performed. The study population was an incident cohort of childhood-onset insulin-dependent diabetic (IDDM) subjects whose duration of IDDM was ≥25 yr (n = 175).

RESULTS— Patients with macrovascular disease ($P < 0.01$) or nephropathy ($P < 0.05$) reported significantly poorer quality of life compared with those who were free from all complications. Patients with macrovascular disease also reported greater depressive symptomatology ($P < 0.05$). Quality of life significantly deteriorated according to the presence of multiple (≥4) complications ($P < 0.001$). Higher depression symptom scores were also related to the presence of ≥4 complications ($P < 0.001$). Those with multiple complications reported less type A behavior than those without any complications ($P < 0.05$).

CONCLUSIONS— This study shows that psychosocial differences exist according to both the number and the type of diabetic complications present. Because poorer quality of life and symptoms of depression may both result from complications, prospective follow-up is needed to clarify their temporal interrelationships, and to determine whether type A personality affords any protection against complications or is diminished as a result of developing complications.

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RECEIVED FOR PUBLICATION 13 AUGUST 1990 AND ACCEPTED IN REVISED FORM 3 JULY 1991.

It is recognized that a high proportion of patients with insulin-dependent diabetes mellitus (IDDM) will be affected by one or more diabetic complications at some point during the course of their disease. However, few of these patients appear to avoid major complications altogether. Many studies have examined the characteristics of IDDM subjects who have survived long durations without major complications (1–4), and it has been suggested that good glycemic control is a major factor in the avoidance of complications (5,6). However, none of these studied in a systematic way—with standardized methods of ascertainment—the associations of personality type with complication status or examined the potential influence of complications on quality of life and depressive symptomatology.

Psychosocial factors play an important role in both morbidity and mortality in nondiabetic populations (7,8). Although based on small numbers, studies have suggested that factors such as stress and social support may be implicated in the onset of diabetes (9,10). However, the role that these and other psychosocial factors play in determining morbidity and mortality in diabetic patients has not been clearly defined. Therefore, the aim of this study was to investigate the association of psychosocial factors and the prevalence and number of diabetic complications in a group of patients who have had sufficient (≥25 yr) exposure to diabetes to develop major complications if they are at high risk. In this report, we focused on *1*) the relationship between complications and both quality of life and depressive symptomatology and 2) the association of type A behavior with complications.

RESEARCH DESIGN AND METHODS

— The study population was comprised of participants in the Epidemiology of Diabetes Complications (EDC) Study. This study was

based on the Children's Hospital of Pittsburgh (CHP) IDDM Registry for 1950–1980, a well-defined cohort of IDDM patients diagnosed or seen within 1 yr of diagnosis at CHP. The CHP registry is likely to be representative of the Allegheny County childhood diabetic population because it includes 70% of all patients diagnosed with diabetes before the age of 17 yr in Allegheny County (11). The eligibility criteria for the CHP registry required individuals at onset of diabetes to be *1*) on insulin therapy at hospital discharge and *2*) <17 yr old. There were 657 participants with a mean age and duration of diabetes of 28 and 20 yr, respectively, who met the additional EDC criteria of living within 100 miles of Pittsburgh during the baseline examination, which was conducted between 1986 and 1988. Sixty-seven percent of those eligible agreed to full participation in the study. Details of recruitment and study methodology have been published previously (12). This study concerned the 175 subjects (50% men) with a diabetes duration of ≥25 yr at time of baseline examination. This duration group was chosen *1*) to allow sufficient duration for subjects to develop complications (thus yielding sufficient sample sizes), *2*) to identify a group with clear evidence of low risk for complications, and *3*) to minimize confounding by age and duration per se.

QUESTIONNAIRE DATA — Two weeks before the scheduled appointment, three questionnaires and containers for the collection of 24-h and separate overnight urine samples were mailed to participants. Questionnaires were answered before examination, at which time they were checked for completeness. The questionnaires included medical history and health behavior (including smoking habits, alcohol intake, diabetes management, and monitoring) and a series of psychosocial questionnaires including the quality-of-life questionnaire from the Diabetes Control and Complications Trial (DCCT) (13). The quality-of-life questionnaire was originally designed to assess the patient-perceived burden of different treatment regimens in subjects participating in the DCCT, a trial comparing the efficacy of alternative regimens on the development of diabetic complications. The questionnaire includes scales to measure satisfaction, worry, and the perceived impact of treatment on various aspects of life. The Bortner (14) questionnaire measures the presence of type A or coronary-prone behavior patterns. The characteristics of type A behavior include time-urgent, hard-driving behavior and aggressive competitiveness. The Bortner questionnaire consists of 14 items, each composed of two adjectives or phrases that reflect either type A behavior or the opposite, type B behavior. Subjects are asked to mark on a horizontal line between two phrases where they feel they belong in terms of their own behavior. A total score is obtained by adding the scores for each of the 14 items, so that the higher the score, the more type A the subject. The Beck Depression Inventory (BDI) consists of a 21-item Likert scale that taps specific depressive symptoms, such as feelings of sadness, discouragement, guilt and disappointment, loss of weight and appetite, and disturbed sleep (15). The BDI has been used in both diabetic and nondiabetic populations.

CLINICAL EXAMINATION — On arrival at the clinic in the fasted state, subjects underwent standardized blood pressure measurement (Hypertension Detection and Follow-up Program Protocol [16]) and a blood sample was taken for various determinations, including HbA_1 (saline incubated). A further timed (~4-h) urine sample was obtained during clinic attendance. The three timed urine samples (24-h, overnight, and 4-h clinic) were assayed for albumin and creatinine (17) to calculate the albumin excretion rate, glomerular filtration rate, and albumin-creatinine ratio. After taking their insulin and receiving breakfast, the participants underwent a 12-lead electrocardiogram, had their pupils dilated, and underwent threefield stereo fundus photography. A standardized medical history and clinical examination was performed by a trained internist for assessment of neuropathy (Diabetes Control and Complications Trial Protocol) and cardiovascular disease (18). The internist was unaware of the questionnaire results at the time of exam but was informed of subjects who had a high depression score at the time of the exit interview so that appropriate counseling could be offered. A final urine specimen was collected before the exit interview with the physician.

DEFINITIONS OF COMPLICATION END POINTS — These end points have been fully described previously (12).

Nephropathy

Overt nephropathy was defined as the presence of renal failure (serum creatinine >442 μM or on dialysis or status after renal transplant) or albumin excretion rate (AER) >200 μg/min in two of the three timed urine samples or, in the absence of urine collections, a serum creatinine >176.8 μM. In a few subjects, the adequacy of the timed urines was questionable in terms of the creatinine excretion; in these cases, a previously validated albumin-creatinine urinary ratio was used (i.e., >0.3 mg/mg for overt nephropathy) (17).

Neuropathy

Distal symmetrical polyneuropathy (DSP) was considered present if, in the opinion of the examining physician, at least two of the following three criteria were present and not due to a nondiabetic cause: *1*) symptoms (numbness, dysesthesia and paresthesia, pain, and

Table 1—*Complication status by sex*

	TOTAL POPULATION (*N* = 175)	MEN (*N* = 88)	WOMEN (*N* = 87)
NO COMPLICATIONS	32 (18)	15 (17)	17 (19)
PROLIFERATIVE RETINOPATHY	110 (63)	64 (73)	46 (53)*
MACROVASCULAR DISEASE	40 (23)	13 (15)	27 (31)†
OVERT NEPHROPATHY	64 (37)	42 (48)	22 (25)*
NEUROPATHY	102 (58)	55 (63)	47 (54)

Values were assessed by Student's *t* test with percentages in parentheses. Subjects may have had >1 complication.
*$P < 0.05$ for comparison by sex.
†$P < 0.01$.

hypersensitivity to touch) consistent with DSP; 2) decreased (i.e., requiring reinforcement) or absent tendon reflexes; and 3) signs of sensory loss (light touch, pinprick, and vibratory perception [tuning fork] examination). Although symptoms of autonomic neuropathy and symptoms and signs of motor neuropathy were documented, the frequency of these abnormalities was insufficient to permit further analysis alone.

Retinopathy

Stereo fundus photographs were taken of fields 1, 2, and 4 and were read by the Fundus Photography Reading Center at the University of Wisconsin (Madison, WI). Readings were classified according to the modified Airlie House System (19). Proliferative retinopathy was determined by grade ≥60 in at least one eye, or if individuals without fundus photographs gave a history (with confirmation by their ophthalmologist if needed) of proliferative change.

Macrovascular disease

Definite macrovascular disease was considered present if any of the following criteria were met. *Peripheral vascular disease (PVD)*—an ankle-arm blood pressure ratio <0.8 was detected either at rest or after exercise or a history of amputation for peripheral vascular disease. *Cardiovascular disease (CVD)*—a history of myocardial infarction (MI) was elicited that was confirmed by either electrocardiographic changes (i.e., pathological Q waves at the time of exam), or if review of previous hospital records met the criteria of the Community Cardiovascular Surveillance Project Study (CCSP) (20) for definite MI, or if a history of angina or stroke was determined by the examining physician. Four individuals reported strokes, three of whom also had coronary artery disease, i.e., MI or angina.

LABORATORY DETERMINATIONS

— HbA_1 was originally determined with saline-incubated blood samples and microcolumn cation-exchange chromatography (Isolab, Akron, OH). On 26 October 1987, the HbA_1 technique was changed to high-performance liquid chromatography (Diamat, Bio-Rad, Hercules, CA). Extensive duplicate samples were run with both techniques, and no systematic differences were seen. Readings with the two methods were almost identical ($r = 0.95$; Diamat $[HbA_1] = -0.18 + 1.00$ Isolab $[HbA_1]$). The difference between the means of the two methods was 0.158.

Statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS). Student's *t* test, analysis of variance (ANOVA), χ^2 test, and multiple logistic regression, with forward stepping, were performed to test for independent associations between the variables. With forward stepping, variables were entered into the equation one at a time. At each step, the independent variables not yet entered were examined and entry was determined by meeting a preset tolerance test and *F* value criteria. Forward stepwise regression was chosen because it is particularly suited to analysis when there is a high proportion of variables in the model in relation to the number of cases.

RESULTS — Table 1 shows the prevalence of the four major complications in the 175 subjects who had diabetes for ≥25 yr. Only 32 (18%) of these subjects had none of the advanced complications; 11 (6%) had all four complications. Differences in complications by gender are also shown in Table 1. More men than women had proliferative retinopathy and nephropathy ($P < 0.01$). Women were more likely to have macrovascular disease than men ($P < 0.05$), largely a result of excess PVD in women. Table 2 shows mean age, duration of diabetes, and HbA_1 level by complication status. Participants with each of the complications had significantly higher mean HbA_1 levels ($P < 0.01$) and longer duration of diabetes compared with those who were free from complications ($P < 0.05$).

Quality of life

The quality of patients' lives was significantly related to the presence of certain diabetic complications (Table 3). In these analyses, subjects with a specific complication (who may have had multiple complications) were compared with the group with no complications at all. Patients who had macrovascular disease or nephropathy reported significantly poorer quality of life compared with those who were free from all com-

Table 2—*Mean age, duration (yr), and HbA_1 by complication status*

	AGE (YR)	DURATION (YR)	HbA_1 (%)
NO COMPLICATIONS	36.0 ± 4.8	28.3 ± 2.4	9.2 ± 1.2
PROLIFERATIVE RETINOPATHY	36.4 ± 4.6	29.6 ± 3.1*	10.4 ± 1.8‡
MACROVASCULAR DISEASE	38.0 ± 4.6	29.9 ± 2.7*	10.4 ± 1.9†
OVERT NEPHROPATHY	36.5 ± 5.1	29.7 ± 3.2*	10.5 ± 1.9‡
NEUROPATHY	37.3 ± 4.4	30.0 ± 3.0†	10.6 ± 1.8‡

Values are means ± SD by Student's *t* test. Subjects may have had >1 complication.
*$P < 0.05$, †$P < 0.01$, and ‡$P < 0.001$, complications vs. no complications.

plications (mean scores on QL questionnaire: 35.1 vs. 30.1, $P < 0.01$ and 33.6 vs. 30.1, $P < 0.01$, respectively). These findings were independent of the effect of sex, duration of diabetes, or glycemic control. When PVD and CVD were examined separately, those with PVD reported a significantly poorer quality of life compared with patients who were free of all complications (35.4 vs. 30.1, $P < 0.01$). Subjects with CVD also reported a poorer quality of life compared with complication-free subjects (36.3 vs. 30.1, $P < 0.01$).

Quality of life significantly deteriorated according to the number of complications present (see Table 4), with a mean QL score of 30.1 for those free from complications compared with a mean score of 38.3 for those with all four complications ($P < 0.01$).

A multiple regression analysis adjusted for sex, duration, and glycemic control demonstrated that the presence of nephropathy was the most important independent predictor of quality of life (β coefficient = 0.19, $P < 0.05$) (Table 7).

Depression

The presence of depressive symptomatology, as measured by BDI, was highly correlated with quality of life ($P < 0.01$) and was also significantly related to the presence of diabetic complications (Table 3). Although those with macrovascular disease or neuropathy or nephropathy all had higher BDI scores (i.e., greater frequency of symptoms), when compared with those who were free from complications, the difference was only significant for those with macrovascular disease ($P < 0.05$). Similar significant findings were observed when PVD and CVD were examined separately, with subjects with these complications having higher BDI scores compared with subjects without complications (11.1 vs. 7.4, $P < 0.01$ and 14.3 vs. 7.0, $P < 0.001$, respectively).

Overall, women had higher BDI scores than men ($P = 0.06$). Thus, analyses were repeated for men and women separately. Among women, there were no differences in the scores of those with and without complications, although women with CVD had higher BDI scores compared with women without complications (12.3 vs. 7.0, $P < 0.06$). Men with macrovascular disease reported higher depressive symptomatology than men who were free from complications ($P < 0.01$). More specifically, men with CVD had significantly higher BDI scores compared with men free from complications (15.8 vs. 6.8, $P < 0.01$). Men with PVD did not have significantly higher BDI scores compared to complication-free men.

Higher BDI scores were significantly related to the number of complications present (Table 4), with a mean BDI score of 6.9 for those without complications compared with a mean score of 13.8 for those with all four complications ($P < 0.01$). A multiple regression analysis in which the four complications and the interaction terms between the different complications were entered into the same model demonstrated that patients who had both retinopathy and macrovascular disease were most likely to have the greatest depressive symptomatology ($P < 0.01$) (Table 7).

Type A behavior

Type A behavior was not significantly correlated with either depressive symptomatology or quality of life. Type A scores on the Bortner scale did not differ significantly between the groups with complications and the group without (Table 5). However, the number of complications present was significantly related to Bortner scores, with the lowest mean type A scores seen in those

Table 3—*Quality of life and depressive symptomatology by complication status*

	QUALITY OF LIFE	DEPRESSIVE SYMPTOMATOLOGY
NO COMPLICATIONS	30.1 ± 3.9	6.9 ± 5.4
RETINOPATHY	32.2 ± 12.1	7.8 ± 7.2
MACROVASCULAR DISEASE	35.1 ± 14.5*	10.9 ± 8.0†
NEUROPATHY	32.0 ± 12.8	9.0 ± 7.5
NEPHROPATHY	33.6 ± 11.8†	8.5 ± 7.0

Values are means ± SD by Student's *t* test. Covariates were duration of diabetes, sex, and HbA_1 level.
*$P < 0.01$, †$P < 0.05$, complications vs. no complications.

Table 4—*Quality of life and depressive symptomatology by number of complications*

	QUALITY OF LIFE	DEPRESSIVE SYMPTOMATOLOGY
NUMBER OF COMPLICATIONS		
NO COMPLICATIONS (N = 32)	30.1 ± 3.9	6.9 ± 5.4
1 (N = 37)	29.0 ± 10.8	8.9 ± 6.8
2 (N = 45)	30.5 ± 11.2	5.7 ± 4.4
3 (N = 48)	33.3 ± 13.5*	9.5 ± 8.5†
4 (N = 11)	38.3 ± 12.9‡	13.8 ± 6.8‡

Values are means ± SD by analysis of variance, adjusted for multiple comparisons. Covariates were duration of diabetes, sex, and HbA_1 levels.
*$P < 0.01$, †$P < 0.05$, ‡$P < 0.001$, complications vs. no complications.

who had all four complications (Table 6). The mean Bortner score in those without complications was 193.7 and for those with all four it was 178.4 ($P < 0.01$). A multiple regression analysis, in which all complications, sex, duration, HbA_1 and a new variable measuring the presence of two or more complications were entered into the model, demonstrated that the presence of two or more complications was a crucial factor in determining lower type A scores. When interaction terms were entered into the regression model, subjects with both retinopathy and macrovascular disease had the lowest Bortner scores ($P < 0.01$) (Table 7).

CONCLUSIONS— This study showed that both quality of life and depressive symptomatology are significantly related to complication status. Quality of life is especially affected by the presence of nephropathy. Areas of life that were reported to be the most affected (and this was true for all complications) were driving, working machinery, exercising, sexual behavior, missing work or school, and carrying out household duties (data not shown). A test for linear trend demonstrated that the number of complications present was significantly related to patients' quality of life, with quality gradually deteriorating as more complications developed ($P < 0.001$).

The frequency of depressive symptoms also became higher with the greater number of complications present (test for linear trend was significant at $P < 0.05$). The most significant independent predictor of depression was the combination of retinopathy and macrovascular disease. The relationship between depression and macrovascular disease was explained by the presence of CVD, especially in men. This could be associated with more obvious symptomatology compared with PVD. Some studies have suggested that depressive symptomatology is not related to complication status (21,22). Lustmann et al. (21) demonstrated comparable rates of retinopathy, neuropathy, and nephropathy in groups of depressed and nondepressed diabetic patients (21). Other research refutes this, showing the presence of complications to be related to psychiatric symptomatology (23,24), and our results support this latter work. However, it is unknown whether the development of complications leads to depression, or whether depression exacerbates the development of complications. This may take place via effects of depressive symptomatology on regimen adherence and coping behavior, which may in turn affect glycemic control. Alternatively, depression and complications may appear at the same time due to some other factor such as stress.

In our study, type A behavior was measured by a self-report questionnaire, and we did not find a difference in scores between subjects with complications and those without complications. However, the number of complications present appears important, because a test for linear trend was significant ($P < 0.001$). Lower type A scores were significantly predicted by the presence of multiple complications. In addition, we found some relationship between lower type A scores and the coexistence of both retinopathy and macrovascular disease.

Studies in diabetic populations have also been inconclusive, with one study failing to find any correlation between type A Bortner scores and the presence of complications (25). This

Table 5—*Type A behavior by complication status*

	BORTNER SCALE
NO COMPLICATIONS	193.7 ± 63.4
RETINOPATHY	179.1 ± 61.0
MACROVASCULAR DISEASE	179.7 ± 80.7
NEUROPATHY	178.6 ± 65.1
NEPHROPATHY	179.7 ± 46.1

Values are means ± SD by Student's t test and were not statistically significant. Covariates were duration of diabetes, sex, and HbA_1 level.

Table 6—*Type A behavior and number of complications*

	BORTNER SCORE
NO. OF COMPLICATIONS	
NO COMPLICATIONS	193.7 ± 63.4
1	204.0 ± 58.2
2	176.0 ± 67.7*
3	174.1 ± 61.2*
4	178.4 ± 61.3*

Values are means ± SD by analysis of variance, adjusted for multiple comparisons. Covariates were duration of diabetes, sex, and HbA_1 level.
*$P < 0.05$ complications vs. no complications.

Table 7—*Multiple regression analyses of insulin-dependent diabetic complications as predictors of quality of life, depression, and type A score*

	R	SE	P
QUALITY OF LIFE			
NEPHROPATHY	0.19	0.95	0.0158
DURATION OF DIABETES	0.02	0.03	0.7552
SEX	0.01	1.81	0.9116
HbA_1	−0.05	0.52	0.5009
DEPRESSION			
MACROVASCULAR (RETINOPATHY)	0.24	1.48	0.0023
DURATION OF DIABETES	−0.02	0.01	0.7628
SEX	0.15	1.03	0.0566
HbA_1	−0.05	0.30	0.5028
TYPE A SCORE*			
MACROVASCULAR (RETINOPATHY)	−0.24	13.99	0.0018
DURATION OF DIABETES	−0.09	0.14	0.2394
SEX	0.05	9.72	0.5246
HbA_1	−0.08	2.85	0.3007

* As measured by Bortner questionnaire.

difference from our findings may be partially due to the smaller sample size and shorter duration of diabetes in that study's population (25).

It is possible that in the EDC Study we are witnessing a protective effect of some aspect of behavior on the development of complications. In previous studies, it has been demonstrated that type A behavior patterns may lead to different health behaviors; this has also been linked to education level and social class (26). In our study, we found that those with higher education levels and those in higher income brackets had fewer complications. This needs to be explored further. It is also possible that the development of complications leads those with diabetes to adopt less competitive, less aggressive (and therefore less type A) behavior patterns. Learning to cope with the disabling effects of complications, and the possibility of improving quality of life for the individual patient, are important issues that urgently need to be addressed. It may be that intervention is required to manage the social implications of diabetes in addition to its clinical management.

Although previous studies have examined the effect of diabetes per se on quality of life and depression, this study shows that it may be important also to look within the diabetic population for differences due to complication status, both number and type. Our study has demonstrated that these differences do exist, and raises the possibility that type A behavior may also affect whether these complications develop. We report only the findings at baseline and, therefore, it is difficult to ascertain the direction of the associations between these factors. However, because this study is now embarking on a follow-up phase, it will be possible in the future to assess more carefully whether these psychosocial differences precede the development of complications.

Acknowledgments— This work was supported by National Institutes of Health Grant DK-34181.

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