Eating Disorder and Type 1 Diabetes: Overview and Summing-Up

Søren Nielsen1* and Anne Grethe Mølbak2
1Department of Child Psychiatry, Rigshospitalet, and Psychosomatic Unit, Department of Child and Adolescent Psychiatry, Bispebjerg Hospital, University of Copenhagen, Denmark
2Steno Diabetes Center, Gentofte, Denmark

The subject of concurrent eating disorder (ED) and insulin-dependent diabetes mellitus (IDDM) has attracted considerable attention for more than a decade. This paper is the first attempt at a quantitative summary of this field. Uncontrolled studies and anecdotal reports suggest an increase of ED in IDDM patients, and also an increase of IDDM in ED patients. Reviews and case reports underscore the difficulty of treating patients with both disorders, the early occurrence of neurovascular complications in these patients and the need for controlled studies. Meta-analysis of five controlled studies do not support an hypothesis of increased risk of ED in female IDDM patients for any type of ED: (anorexia nervosa, AN; bulimia nervosa, BN; unspecified or subclinical ED, ED-NOS). Findings from register studies do not support an hypothesis of increased occurrence of IDDM in female AN-patients. An hypothesis of increased risk of retinopathy is supported by two controlled studies. The interest in concurrent ED and IDDM is thus not justified by any increase in concurrence, but in the early occurrence of clinically significant retinopathy (OR 8.04; 95 per cent CI 4.0–16.1), and other diabetic complications. The existing studies do not seem to have taken full advantage of existing diabetes-specific knowledge, whereas knowledge related to the eating disorders are fully incorporated. Future epidemiological studies should be cause-seeking rather than merely descriptive. These studies should try to relate risk factors, protective factors and specific risk behaviours with health outcome i.e. complications and mortality. © 1998 John Wiley & Sons, Ltd and Eating Disorders Association.

Keywords: eating disorder; type 1 diabetes; co-morbidity; epidemiology; review; metanalysis

*Correspondence to: Søren Nielsen, MD, Child Psychiatrist, Dronning Sofies Vej 89, DK-4000 Roskilde, Denmark.
INTRODUCTION

‘We shall perhaps not so soon see’ (Finnegans Wake, James Joyce)

Since the earliest references to concurrent diabetes mellitus and eating disorder (Bruch, 1974; Crisp, 1977) and the appearance of the first case report (Adin and Nelken, 1978) almost one hundred cases have been described (please see references marked *) and there have been a number of surveys and special studies. The subject of such ‘dual diagnosis’ is beginning to get attention in textbooks on diabetes mellitus (Drash and Becker, 1990; Steel, 1991; Pickup, 1992; Vinik and Wing, 1992) and on eating disorders (Rodin et al., 1993; Peveler, 1995; Treasure and Szmukler, 1995; Carney and Andersen, 1996; Powers, 1996).

The general psychological difficulties of adjusting to diabetes mellitus have been appreciated for some time (please see references marked †). However, this does not mean that diabetologists necessarily find psychiatrists helpful in the management of ‘difficult’ cases (Tattersall, 1981). Nevertheless, the particular problem of coincident diabetes and eating disorder seems to present special issues and difficulties. The unresolved problem of how much concurrence is thus of more than academic interest. Concurrence of eating disorder and diabetes mellitus leads to deterioration of both conditions (Adin and Nelken, 1978; Colas et al., 1991; Feiereis, 1988; Hillard et al., 1983; Hillard and Hillard, 1984; Nielsen et al., 1987; Steel et al., 1987). Treatment regimens for both disorders need modifications. Treatment is generally considered difficult (Popkin, 1989; Rodin and Daneman, 1992), but some promising approaches are being developed (Peveler and Fairburn, 1989, 1992; Ramirez et al., 1990).

There have been eight previous reviews of eating disorders and diabetes (see below), however, none has used formal meta-analytic methods. The present review has three parts: an introductory narrative review, a quantitative summary including meta-analysis and finally, information derived from independent Danish register studies is used to demonstrate the merits and shortcomings of this approach.

INTRODUCTORY REVIEW

The literature on diabetes and eating disorders is growing. Cases have been reported in 22 papers. (These papers are listed and marked with * in the reference list.) The studies of eating disorders in diabetes mellitus (marked ‡ in reference list), seem in general to be methodologically more sound than the six studies which examine diabetes in eating disorders (marked § in the reference list).

Previous reviews

Eight narrative reviews have been published (Butler and Wing, 1994; Hillard and Hillard, 1984; Marcus and Wing, 1990; Nielsen et al., 1987; Nieuwenhuijzen Kruseman, 1991; Popkin, 1989; Rodin and Daneman, 1992; Vila et al., 1994).

Popkin (1989) correctly remarks of the then existing studies that ‘collectively the studies leave much to be desired’. Nevertheless, there is much of clinical value in these studies. Rodin and Daneman (1992) touch upon many central themes of the problem. They make it clear that a degree of eating disorder which in general would be considered ‘subclinical’, in female IDDM cases might well be a problem worth the effort and skill of the clinician because of the deleterious effect on the regulation of IDDM, and the risk of early and severe ocular (and other neurovascular) complications. Their paper goes into methodological issues, manner of presentation, explanations and mechanisms behind the association of ED and IDDM, and, last but not least, case management. Vila et al. (1994) use two perspectives, one the prevalence of IDDM in psychiatric ED-populations, the other the prevalence of ED in IDDM populations. The paper contains a good discussion of bias and heterogeneity in the published reports. The authors’ conclusion, that it is at present impossible to give reliable figures, is largely because they do not include any papers published after 1990 and so omit the best controlled studies. However, the paper contains a good discussion of clinical difficulties and the interaction between ED, the levels of glycosylated haemoglobin (HbA1c) and early occurrence of neurovascular complications. Popkin (1989) suggests that bulimia nervosa may be a possible perpetuating factor in pancreatitis. The review part in Nielsen et al. (1987) focuses on emotional development and diabetes from a basically psychodynamic and pedagogical perspective. Their interpretation of the prevalence estimate seems flawed, as the authors have not taken the 25-year cumulation period into account. This problem will be attended to in a later section of the present paper.

Surveys—general comments

The surveys published so far have by and large used satisfactory methodology for eating disorders, but are rather less satisfactory with respect to diabetes. Johnson (1988) has discussed these shortcomings and made many important recommendations. Most authors to date have used existing instruments when evaluating eating disorders or general psychopathology. None seems to have taken full advantage of the existing knowledge on diabetic patients’ variables, nor have they used instruments developed for the analysis of diabetes-specific behaviour (Bradley, 1994). The use of general measures instead of specific tools is likely to lead to loss of information.
There have been a number of surveys of general psychopathology in IDDM populations (Lustman et al., 1986; Popkin et al., 1988), but some have not included eating disorders as specific categories for study (Wilkinson et al., 1987, 1988).

Studies of eating disorders in IDDM populations

There have been 15 such studies and some characteristics and results of these are summarized in Table 1. Most were observational studies but some were controlled. Of the controlled studies five (Robertson and Rosenvinge, 1990; Fairburn et al., 1991; Striegel-Moore et al., 1992; Peveler et al., 1992; Vila et al., 1995) were judged to approach an optimal methodology in that they had sufficient numbers of females in the relevant age group, used a relevant control group, used clinical interview as a supplement to self-report measures (all subjects), recorded relevant physiological variables (glycosylated haemoglobin, height and weight), and conducted power analyses. These will be included in later meta-analysis. Popkin et al. (1988) is also a well-controlled study but its subjects were candidates for pancreas transplantation. Lustman et al. (1986)

Table 1. Eating disorders in type 1 (insulin-dependent) diabetes

<table>
<thead>
<tr>
<th>Source</th>
<th>‘Clinical’</th>
<th>‘Subclinical’</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AN</td>
<td>B</td>
</tr>
<tr>
<td>Lustman et al. (1986)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rodin et al. (1986)†‡</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Rosmark et al. (1986)*‡‡</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Steel et al. (1987)‡§</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Popkin et al. (1988)*</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Powers et al. (1990)†‡</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Robertson and Rosenvinge (1990)*‡§</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fairburn et al. (1991)*‡§</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Striegel-Moore et al. (1992)*‡§</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Peveler et al. (1992)*‡§</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rosenvinge and Vaglum (in preparation)*‡§</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Pollock et al. (1995)†</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Vila et al. (1995)*‡§</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Affenito et al. (1997)‡§</td>
<td>4</td>
<td>10</td>
</tr>
</tbody>
</table>

*Controlled study. †Observational study. ‡Sole reliance on self-report questionnaires. §Clinical interview. ||Affenito (1997).
controls for type of diabetes. The results of these studies are not easily
generalized and were therefore left out of the meta-analysis.

However, other studies did have findings which are of interest. Marcus et al. (1992) in a registry-based study of IDDM-patients, found that the 153 (80.4 per cent of 188 eligible) who completed the BULIT (Smith and Thelen, 1984) and EDI (Garner et al., 1983) questionnaires, were comparable to those of nondiabetic standardization samples with respect to eating disorder symptomatology. However, eating disorders symptomatology was associated with poorer control of diabetes. Steel et al. (1987) studied 208 women followed regularly at a diabetes clinic at a university hospital for 8 years and found that 12 had anorexia nervosa and three bulimia nervosa. There was a high incidence and early onset of diabetic complications. Eleven of the 15 eating disordered patients had retinopathy (six with proliferative changes), six had nephropathy and six neuropathy. The study of Rodin et al. (1991) showed the significance of differences in diagnostic systems. They studied a sample of 121 consecutive female patients, age 13–18 years, with IDDM for at least a year. Eighty-five per cent took part in the study. Of these 13 received a DSM-III ED-diagnosis (one anorexia nervosa and 12 bulimia). These figures changed when the DSM-III R diagnostic system was employed—only five of the DSM-III ‘bulimia’ cases fulfilled the stricter DSM-III R criteria for bulimia nervosa. A later follow-up (Ry dall et al., 1997) of this cohort is difficult to compare with the other studies of ED in IDDM, as it employs an idiosyncratic definition of eating disorders (Williams and Gill, 1997). Eating disorders were classified into the following, mutually exclusive categories: highly disordered eating, moderately disordered eating and non-disordered eating, dependent on bingeing, misuse of insulin, vomiting and laxative abuse. About one-third was eating disordered at baseline. This persisted in one-fifth and improved in one-tenth at the 4- to 5-year follow-up. At follow-up one in eight of the normal eaters at baseline had developed disordered eating. Retinopathy was found in 86 per cent of those with highly disordered eating, in 43 per cent of the moderately eating disordered and in 24 per cent of the non-eating disordered at follow-up. A problem is that retinopathy was not evaluated at baseline. Affenito et al. (1997) recruited 90 subjects with an average duration of IDDM of 14.8 years, who were about 90 per cent of the eligible cases (Affenito, 1997), from diabetes clinics throughout Connecticut and Massachusetts over a 3-year period. Fourteen had a clinical DSM-III R eating disorder (AN = 4; BN = 10), 13 had a subclinical eating disorder (ED-NOS(r) = 7; ED-NOS(b) = 6), and 63 were free of ED. The existence of ED was determined by the EDE interview (Cooper and Fairburn, 1987; Cooper et al., 1989) and the BULIT-R inventory (Thelen et al., 1991; Welch et al., 1993). Women with clinical and subclinical ED had elevated HbA1c results and more diabetes-related complications than those without ED. Seventy-one per cent of the clinical group were misusing insulin at the time.
of the study versus 15 per cent of the subclinical group. In both groups more than 75 per cent reported past insulin misuse.

Indeed, it seems well known among diabetic women that omission of insulin is an efficient weight-reducing device (Affenito et al., 1997; Biggs et al., 1994; Birk and Spencer, 1989; Drash and Becker, 1990; Hudson et al., 1983; Mathieu, 1989; Pollock et al., 1995; Polonski et al., 1994; Rodin et al., 1991). We have not found any reports of this behaviour in male IDDM cases. Mathieu (1989) offers some striking psychodynamic formulations as well as verbatim extracts from patients (e.g. a female bulimic who says ‘for once the diabetes is useful to me’—meaning the possibilities for osmotic purge via reduction in insulin). Regrettably, Mathieu (1989) does not report any epidemiological details of his study.

Studies of IDDM in ED populations

Five of the six studies known to us are observational studies. In a large series of AN-patients Gomez et al. (1980) reported finding two cases of concurrent AN and IDDM. Both were females. The series cumulation period was not stated. Powers et al. (1983) found four female IDDM cases in a series of 100 AN patients, cumulated over a period of 8 years. Nielsen et al. (1987) reported finding five female cases of concurrent ED and IDDM in a series of 242 ED patients cumulated over 25 years at a tertiary referral centre. Four cases were AN patients, and one bulimic. Feiereis (1988) cumulated a series of 547 ED patients in a 5-year period. Eleven of these (one male case) also had IDDM. All had bulimia nervosa. Emborg (1996) conducted a nationwide hospital admission register study, employing record linkage. The study covered the years 1970 to 1993, i.e. the period where the ICD-8 diagnostic system was used in Denmark. After 1977 both the somatic and the psychiatric admission registers were computerized. In this 17-year period 29 cases of IDDM were found amongst 2295 ED patients (Emborg, 1997). Findings from these studies are summarized in Table 2.

The concurrent cases are not distributed homogeneously across samples (chi-square 9.64; df 4; p = 0.05). Overall, of these series of ED patients 1.4 per cent had IDDM (range: 0.5–4.2 per cent). The sixth study (Ward et al., 1995) is a case–control study of a consecutive series of diabetes patients seen at the Maudsley Hospital Eating Disorders Unit between January 1990 and June 1994 (n = 21). Controls were non-diabetic eating disorder patients, matched for eating disorder diagnosis, age at onset and duration of illness, and seen within the same time period. Controls were found for, in all, 17 cases; the remaining four cases were atypical. Of the 17 cases, 11 had bulimia nervosa, five anorexia nervosa and one was an obese binge-eater. Eleven of the 17 cases had diabetic complications (seven eye disease, six peripheral neuropathy, four autonomic neuropathy, and one necrobiosis lipoidica). This study is unique in
that five women were analysed with bone densitometry and all five had osteoporosis. The authors raise the question whether co-morbid diabetes makes severe osteoporosis more likely in anorexia nervosa patients. This study does not appear in the tables on prevalence as it is impossible to say anything epidemiologically meaningful without information about the characteristics of the patient pool of the two clinics involved.

Other authors have reported a high frequency of neurological and vascular complications (see below).

**QUANTITATIVE ANALYSIS**

The following section will use quantitative methods to evaluate the literature on the following topics. When ED and IDDM coincide, which disorder comes first? What are the ages of onset of the disorders? At what rates do ED and IDDM coincide? Is there evidence for an increased risk of neurovascular complications?

**Method of literature search**

An *ad hoc* survey of reference lists of the existing literature was supplemented by a MEDLINE search using combinations of the words ‘eating disorder’, ‘anorexia nervosa’, ‘bulimia’ and ‘bulimia nervosa’ with ‘insulin-dependent diabetes mellitus’. The period 1984–October 1997 is also surveyed by CD-ROM (MEDLINE EXPRESS). Although some unpublished studies are located, publication bias is a very real possibility. This type of bias generally tend to exaggerate the effect estimates (odds ratios). Exclusion or inclusion of a given publication depends on the question under analysis. A
precise listing of papers is given in each subsection of the meta-analysis. Some publications appear in more than one section.

**Statistical methods and data handling**

The number of studies is limited, so there is no need for the more sophisticated ‘computational exercises’ (Greenland, 1987). Following Peto (1987), the main emphasis will be on the simple comparison of the observed and expected (O-E), as this is sensitive to any real effect, understandable, justifiable, clearly unbiased, and assumption-free. The studies in this meta-analysis do not show gross imbalance in number of subjects in the groups, and the estimated odds ratios are not far from unity, so Peto’s method should work well (Fleiss, 1993). The (O-E) approach not only leads to a test of the null hypothesis, but also to a description of the alternative hypothesis. When combining studies we followed the method called ‘Blocking the data’ by DeMets (1987). Mantel–Haenszel’s (1959) chi-square and Miettinen’s (1976) approximative method is used for computing the combined odds ratio (OR) with its corresponding 95 per cent confidence interval (95 per cent CI). The actual computations have been performed by the CIA—Confidence Interval Analysis—program by Gardner et al. (1992), using the methods outlined in Gardner and Altman (1989). Exact p-values are computed using the ‘probability functions’ facility in the STATISTIX (1996) computer package. Greenland (1987) underscores the importance (and limitations) of a statistical test for heterogeneity as a necessary first step in the analysis: a small p-value indicates that heterogeneity should not be ignored, but on the contrary explored. A large p-value does not indicate that heterogeneity can be safely ignored. Peto (1987) cautions that the degree to which results from meta-analysis can be reasonably extrapolated, is a matter of judgment rather than precise mathematical calculation. When testing for heterogeneity we use the G-test (Sokal and Rohlf, 1981), a chi-square distributed log-likelihood-ratio criterion of goodness of fit. Further statistical details appear in the relevant subsections.

**RESULTS**

**Which disorder comes first?**

The order of onset is of interest when evaluating the influence of one disorder on another. Twenty-two papers contain the necessary information (Bruch, 1974; Adin and Nelken, 1978; O’Gorman and Eyre, 1980; Fairburn and Steel, 1980; Gomez et al., 1980; Garner, 1980; Roland and Bhanji, 1982; Hillard et al., 1983; Powers et al., 1983; Hudson et al., 1983; Szmukler, 1984; Hardoff et al., 1984; Sreenivasan, 1984; Brooks, 1984; Malone and Armstrong, 1985; Rodin et al., 1986; Nielsen et al., 1987; Steel et al., 1987; Feiereis, 1988;
Pollock et al., 1995; Ward et al., 1995). These studies give relevant information on 94 cases. IDDM occurred more than 1 year before ED in 81 cases, in the same year in four cases, and more than 1 year after ED in nine cases. The sign test (Armitage and Berry, 1987) yields a chi-square = 56; df 1; \( p < 0.00001 \). Thus IDDM appeared before ED in the majority of published cases. Taken alone this finding seems to indicate that IDDM is a strong risk factor for developing ED in young females.

**Age at onset of IDDM and AN**

Fifteen studies contain the information necessary for this analysis (Adin and Nelken, 1978; Fairburn and Steel, 1980; Gomez et al., 1980; Garner, 1980; O’Gorman and Eyre, 1980; Roland and Bhanji, 1982; Powers et al., 1983; Hillard et al., 1983; Hudson et al., 1983; Szmukler, 1984; Hardoff et al., 1984; Brooks, 1984; Malone and Armstrong, 1985; Nielsen et al., 1987; Feiereis, 1988). A total of 43 cases are reported. Age at onset of IDDM and AN is shown in Table 3 below.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>IDDM</th>
<th>AN/B</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>5–9</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>10–14</td>
<td>25</td>
<td>7</td>
</tr>
<tr>
<td>15–19</td>
<td>7</td>
<td>27</td>
</tr>
<tr>
<td>20–24</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>25–29</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Assuming that the distribution of age at onset of the respective disorders is the same as found in the register study reported in this paper, the results of formal testing are as follows: AN—\( \text{Gadj} = 4.415; \text{df} \ 2; \ p = 0.11, \text{n.s.} \); IDDM—\( \text{Gadj} = 31.815; \text{df} \ 4; \ p < 0.00001 \). Thus age at onset of eating disorders is not significantly different from the expected, whereas age at onset of IDDM is; too many cases being found in the age group 10–14 years, and too few in the age groups 0–10 and 25–29 years. (The difference will stand out even more if Table 3 is compared to Figure 2 in the register part of this paper.) When this result is combined with the findings on order of appearance, the best explanation seems to be publication bias, but the possibility that developing IDDM at age 10–14 years is a strong predictor of later development of ED in female IDDM cases must also be considered.
Occurrence of ED in IDDM populations

Fourteen papers are relevant (see Table 1 above). There is a significant amount of heterogeneity in these studies. Some are cross-sectional surveys, others are controlled studies. Some have clearly unsatisfactory methods or response rates. On average anorexia nervosa (AN) is reported in 2.7 per cent IDDM patients (range 0–7.3 per cent). The comparable figure for bulimia is 3.7 per cent (range 0–11.1 per cent). Bulimics are not distributed homogeneously across all 14 studies (chi-square = 31.15; df 13; p = 0.003), but among the controlled studies we could not detect significant heterogeneity (chi-square = 5.62; df 5; p = 0.34).

Using the combined results of the five studies where this was judged to be legitimate as discussed above (Robertson and Rosenvinge, 1990; Fairburn et al., 1991; Striegel-Moore et al., 1992; Peveler et al., 1992; Vila et al., 1995) testing for heterogeneity gives the following results: AN (chi-square = 2.49; df 4; p = 0.65, n.s.), BN (chi-square = 5.47; df 4; p = 0.24, n.s.), ED-NOS (chi-square = 36.29; df 4; p < 0.0001). However, the findings for ED-NOS are put in perspective when all information from these five controlled studies is examined using odds ratios. Neither the individual odds ratios (ORs) nor the overall aggregate OR is statistically significant. In all cases the corresponding 95 per cent confidence interval (95 per cent CI) includes unity. (See Fig. 1).

The inclusion and subsequent omission of the Rosmark et al. (1986) study is to illustrate the effect of relying on self-report instruments, as opposed to clinical interviews, on the effect estimates. Apart from the sole reliance on self-report instruments for ED diagnosis, the Rosmark et al. (1986) study is comparable to the other five studies.

Figure 1. Apparent effects of IDDM on occurrence of ED-NOS in five controlled studies. Odds ratio with 95 per cent confidence interval shown for each study. Neither the individual studies nor the overall aggregate finding show any evidence of effect.

Thus combining findings from these studies gives no support for an hypothesis of increased occurrence of ED in IDDM populations. In all diagnostic categories there are no statistically significant differences between diabetics and controls. Given the quality of these studies, the overall finding is that there is no good evidence supporting an hypothesis of increased occurrence of eating disorders in diabetic females. In other words, IDDM is not an effect modifier with respect to the OR for ED.

However, it is worth noting that data from Vila et al. (1995) suggest that the presence or absence of obesity may be an effect modifier in complex ways. Clinical ED was not frequent: two girls had a past history of AN, both in the non-obese group, one diabetic and one nondiabetic. Bulimia only appeared in the IDDM group: two of the 15 obese had bulimia, as did one of 37 non-obese. This is not a statistically significant difference. More frequent was ED-NOS: in IDDM girls ED-NOS was found in nine of 15 obese girls and in 10 of 37 non-obese girls. This difference is statistically significant (chi-square = 5.00; df 1; \( p = 0.025 \)), RR (relative risk) = 2.2 (95 per cent CI 1.13–4.35), OR = 4.05 (95 per cent CI 1.15–14.3). In non-IDDM girls ED-NOS was found in nine of 22 obese girls and in one of 24 non-obese girls, again a significant difference (Fisher’s exact test \( p = 0.004 \) two-tailed). Obesity increases the OR for ED-NOS almost 16-fold (OR = 15.9; 95 per cent CI 1.81–14.0). Obese IDDM girls also had more dysthymia, anxiety disorders, depression and low self esteem than non-obese IDDM girls.

### Occurrence of IDDM in clinical ED populations

None of the five relevant studies (Gomez et al., 1980; Powers et al., 1983; Nielsen et al., 1987; Feiereis, 1988; Emborg, 1996) which are known to us is controlled, and so no firm epidemiological conclusions can be drawn. However, an overall prevalence of 1.4 per cent is found for IDDM in ED populations (range 0.5–4.2 per cent) (see Table 2). Distribution of IDDM across these five studies is not homogenous (chi-square = 9.64; df 4; \( p = 0.05 \)).

---

**Table 4. Concurrent eating disorder in female IDDM patients: summary of meta-analysis**

<table>
<thead>
<tr>
<th>ED diagnosis</th>
<th>Studies (N)</th>
<th>N</th>
<th>O</th>
<th>E</th>
<th>V</th>
<th>OR (95% CI)</th>
<th>Z-score</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AN</td>
<td>6</td>
<td>594</td>
<td>5</td>
<td>2.7618</td>
<td>1.4517</td>
<td>4.67</td>
<td>0.92–23.8</td>
<td>1.86</td>
</tr>
<tr>
<td>AN*</td>
<td>5</td>
<td>493</td>
<td>2</td>
<td>1.544</td>
<td>0.7427</td>
<td>1.85</td>
<td>0.2–17.9</td>
<td>0.53</td>
</tr>
<tr>
<td>B</td>
<td>6</td>
<td>594</td>
<td>8</td>
<td>5.1947</td>
<td>2.6624</td>
<td>2.87</td>
<td>0.86–9.53</td>
<td>1.72</td>
</tr>
<tr>
<td>B*</td>
<td>5</td>
<td>493</td>
<td>7</td>
<td>4.7888</td>
<td>2.4213</td>
<td>2.49</td>
<td>0.71–8.78</td>
<td>1.42</td>
</tr>
<tr>
<td>ED-NOS*</td>
<td>5</td>
<td>493</td>
<td>42</td>
<td>38.945</td>
<td>14.4800</td>
<td>1.08</td>
<td>0.74–2.07</td>
<td>0.80</td>
</tr>
</tbody>
</table>

*Re-analysis omitting the study of Rosmark et al. (1986).
Neurovascular complications in cases with concurrent ED and IDDM

Of the papers which report on neurovascular complications, six allow calculation of rates (see Table 5) but only two permit statistical comparisons with non-ED patients. Overall, significant retinopathy was found in 54 per cent of cases (range 36–73 per cent). There was not a significant amount of heterogeneity across studies (chi-square = 6.51; df 5; p = 0.26, n.s.).

The two controlled studies are Steel et al. (1989) and Colas et al. (1991). Steel et al. (1989) found increase in odds ratio for retinopathy in diabetic subjects (both sexes combined) scoring above 18 on EAT (Garner and Garfinkel, 1979), compared to subjects scoring below 18 (OR = 2.5 (95 per cent CI 1.04–6.1)). Colas et al. (1991) matched for age, duration of diabetes and age at onset of diabetes. Only 38 per cent of diabetic bulimics were free of retinal lesions compared to 80 per cent of the control group. The relative risk (RR) for developing significant retinopathy is 3 for female diabetics who are also bulimia sufferers (RR = 3.00 (95 per cent CI 1.5–5.9)). The odds ratio OR is 6.27 (95 per cent CI 2.0–19.5). When re-analysing the data of Steel et al. (1989) for female probands only (Steel, 1993) OR is 8.63 (95 per cent CI 3.8–19.9). Combining the results of these two studies in the manner described above (DeMets, 1987), yields a common OR of 8.04 (95 per cent CI 4.0–16.1).

Table 5. Frequency of clinically significant retinopathy in cases with concurrent ED and IDDM

<table>
<thead>
<tr>
<th>Source</th>
<th>Retinopathy</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Steel et al. (1987)</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Nielsen et al. (1987)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Colas et al. (1991)</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>Ward et al. (1995)</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Affenito et al. (1997)</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Rydall et al. (1997)</td>
<td>12</td>
<td>9</td>
</tr>
</tbody>
</table>

Key findings

- IDDM appears before ED
- No increase of ED in IDDM populations
- No increase of IDDM in ED populations
- Retinopathy increased (RR = 3) in bulimic diabetics

Summary of findings from meta-analysis

IDDM occurs before ED in the vast majority of cases. Age distribution for onset of AN is typical for AN populations, whereas age at onset of IDDM is not typical of IDDM populations: too many of the concurrent cases have onset of IDDM in the age group 10–14 years. Publication bias is one explanation, another is that getting IDDM at this age is a genuine risk factor for later development of ED. The amount of inter-study heterogeneity in concurrent ED and IDDM is reduced for all three ED diagnoses by restricting analysis to the combinable (DeMets, 1987) studies. The studies approaching optimal design gave the same result: no sign of increased frequency of ED in IDDM for any type of ED. The existing studies of IDDM in ED are rather disparate, and no study was controlled. The heterogeneity of IDDM in ED populations is as expected, given the inter-study differences. Significant retinopathy was found in 54 per cent of concurrent cases, with some heterogeneity across studies. Risk for developing clinically significant retinopathy increases by a factor 3 in bulimic versus non-bulimic diabetics.

REGISTER STUDY

This part of the paper will report the results of using two relevant population-based diagnostic registers to re-examine the issue of the concurrence of IDDM and AN. This may be a useful approach as a supplement to controlled studies, if local registers are sufficiently reliable. However, the results may not be entirely generalizable because both IDDM and ED show considerable geographical variation. As AN is the only specific ED diagnosis in the ICD-8 diagnostic system (WHO, 1965), we had to limit our study to AN.

Method

We studied the region of Greater Copenhagen (Copenhagen and Frederiksberg municipalities and Copenhagen and Frederiksborg Counties). The study population is about 1.5 million people and comprises around one-third of the entire population of Denmark. As male cases are rare in ED, only females have been included in the analyses reported here.

The information on IDDM comes from the register of the Steno Diabetes Center, a specialized diabetes hospital serving this region. The study is focused on juvenile onset (onset before age 30 years) type 1 diabetes. Details of the study are given in Mølbak et al. (in preparation); Christau et al. (1977) and Christy et al. (1979). Ascertainment rate (sampling fraction) is satisfactorily high (462/464 = 0.996). The data on anorexia nervosa originates from a nationwide psychiatric admission register study by the first author (Nielsen,
Sampling fraction 1. The structure of this register is described in Dupont (1983). The population under study does not differ from the entire Danish population with respect to incidence of AN ($G_{\text{adj}} = 0.035$; df 1; $p = 0.85$, n.s.) or age at onset of AN ($G_{\text{adj}} = 1.473$; df 3; $p = 0.67$, n.s.).

The age-specific prevalences of IDDM are computed from cumulated incidence rates. The age-specific prevalence rates ($P$) for AN are derived from incidence rates ($I$) from the region and period of interest using the equation $P = I \times D$, where $D$ is mean duration of illness. One necessary assumption is that $I$ is stable during the period of study and this seems to be the case (Nielsen, 1990). $D$ is estimated as 3.5 years using information from Szmukler and Russell (1986).

**Results**

A graphical presentation of the age-specific prevalences for each disorder is given in Figure 2.

The 1-year prevalences (per 100,000 of the population) for each 5-year age group were set up in $2 \times 2$ tables. The resulting expected prevalences for the cell (+IDDM/ + AN) are tabulated in Table 6 together with the relevant population size, and some derived epidemiological variables. As no case of AN occurred before 5 years of age, only five age groups are reported.

*Figure 2. Diabetes mellitus and anorexia nervosa in Danish females: age-specific prevalence rates. Top panel: insulin-dependent diabetes mellitus. Bottom panel: anorexia nervosa. Note different scaling in the two panels—rectangle at far right indicates the value ‘100’. IDDM increases monotonously whereas AN peaks at age 15–19 years*
Table 6. Expected concurrence of AN and IDDM in Danish females with a numerical example

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Average population (1)</th>
<th>Concurrence* (expected) (2)</th>
<th>Person-years ((1) x (3))</th>
<th>Expected number ((2) x (3)/100,000)</th>
<th>Observed number</th>
<th>Standardized ratio</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-9</td>
<td>48,086</td>
<td>0.001</td>
<td>424</td>
<td>0.055</td>
<td>1</td>
<td>0.50</td>
<td>0.01</td>
<td>0.68</td>
</tr>
<tr>
<td>10-14</td>
<td>48,441</td>
<td>0.035</td>
<td>1,211.025</td>
<td>0.424</td>
<td>0</td>
<td>2.36</td>
<td>0.06</td>
<td>0.68</td>
</tr>
<tr>
<td>15-19</td>
<td>53,488</td>
<td>0.111</td>
<td>1,337.200</td>
<td>0.984</td>
<td>4</td>
<td>2.70</td>
<td>0.70</td>
<td>0.13</td>
</tr>
<tr>
<td>20-24</td>
<td>60,161</td>
<td>0.073</td>
<td>1,504.025</td>
<td>0.998</td>
<td>0</td>
<td>0.50</td>
<td>0.05</td>
<td>0.90</td>
</tr>
<tr>
<td>25-29</td>
<td>61,292</td>
<td>0.024</td>
<td>1,532.300</td>
<td>0.368</td>
<td>0</td>
<td>0.50</td>
<td>0.05</td>
<td>0.90</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>3.386</td>
<td>3,386</td>
<td>55.5</td>
<td>5</td>
<td>0.50</td>
<td>0.05</td>
<td>0.90</td>
</tr>
</tbody>
</table>

*Per 100,000 per year assuming full independence.

Numerical example using Nielsen et al. (1987) dataset.
The null hypothesis of full independence between the two conditions is not refuted. Table 6 is designed to underscore the importance of taking the cumulation period into consideration when interpreting such data. In the original communication from the first author (Nielsen et al., 1987), it was concluded that the finding of five cases in a series of 242 ED probands represented a six-fold increase in prevalence. This was not warranted and it is with some mixed feelings that he hereby remedies his earlier mistake.

CONCLUSIONS

We have not been able to demonstrate any increase in ED in IDDM populations in either our meta-analysis of the results of the more rigorous controlled studies or for AN by the analysis of information obtained from combining two register studies. It seems likely that risk factors and protective factors balance each other out as far as occurrence of ED in IDDM populations is concerned. This also seems to be the case for IDDM in ED populations. However, the interest in concurrent ED and IDDM is justified on clinical grounds. There is evidence for an increased risk (RR = 3) of retinopathy as well as other neurovascular complications in eating disordered female IDDM patients compared to non-ED female IDDM patients. For IDDM patients there seems to be no such thing as ‘subclinical’ eating disorder. IDDM females are not immune to the prevailing feminine stereotype, and they are aware of the weight increasing potential of ‘lege artis’ insulin treatment. All care-persons should expect tough negotiations when defining the optimal care for IDDM females, and some tradeoffs might be necessary. However, it is clear that female IDDM sufferers may pay a high price for trying to live up to the current ideal body shape.

As six well-designed and well-executed studies from different geographical regions give the same result—no major association between ED and IDDM—further descriptive epidemiological studies seem unwarranted. Small degrees of association may exist but would be difficult to detect. Power analysis has shown that a sample size of 1000 cases and 1000 controls would be needed to demonstrate a two-fold increase in prevalence of ED in IDDM (Fairburn et al., 1991). To estimate odds ratios or relative risks the requirements become even more extreme. In order to have 95 per cent confidence in the estimation of a population odds ratio to within 10 per cent of the true value (believed to be in the vicinity of 2) 3041 subjects would be needed in each of the case and control groups (Lemeshow et al., 1988). The difference in prevalence appears to be smaller than this and so it might not be worthwhile trying to establish any differences in such detail. A more promising line of research might be to design a controlled study to elicit which type of disordered eating (and other harmful behaviour) leads to the increase in neurovascular complications in concurrent ED and IDDM. The study by Vila et al. (1995) demonstrates the
importance of controlling for obesity and eliciting eating history. Such research should make use of the increase in precision gained by using instruments such as the Eating Disorders Examination (EDE) (Cooper and Fairburn, 1987; Cooper et al., 1989) for studying features of the eating disorder and the same also applies to the use of the diabetes-specific instruments (Bradley, 1994). Any self-report questionnaires should be completed before the clinical interview, to prevent (or diminish), distortion of information, arising from the proband guessing what the researcher expects. We hope that we have been ‘charting some waters’ (Popkin, 1989) so that our patients might get a safer passage in the future.

ACKNOWLEDGEMENTS

S.N. gratefully acknowledges generous support over a number of years from Fru C. Hermansens Mindelegat, the Snedkermester Axel Wichmann og fru Else Wichmanns Fond, Gangstedfonden and Dansk Psykiatrisk Selskabs Forskningsfond of 1967. A.G.M. acknowledges methodological advice given by the consultant service of the Danish Medical Research Council.

REFERENCES


