

The Impact of Comorbid Depressive and Anxiety Disorders on Severity of Anorexia Nervosa in Adolescent Girls

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Abstract: We examined the impact of comorbid depression and anxiety disorders on the severity of anorexia nervosa (AN) in adolescent girls. Adolescent girls with AN ($N = 88$) were divided into one group with and another group without comorbid disorders, and selected subjective and objective measures of illness severity were compared between the two groups. The comorbid group had significantly higher scores than the noncomorbid group for all four subscales and total scores of the Eating Disorders Examination as well as for all Eating Disorders Inventory–2 subscales, except for bulimia. The comorbid group also had significantly more suicide attempts and hospitalizations compared with the noncomorbid group. There were no significant group differences for the lowest ever body mass index, duration of AN symptoms, and age at AN onset. Our findings suggest that AN with comorbid depression and anxiety disorder is a more severe clinical variant of the disorder, especially with respect to severity of psychological symptoms and suicide risk.

Key Words: Anorexia nervosa, comorbidity, depression, anxiety, adolescent

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Numerous clinical and epidemiological studies have confirmed the clinical impression that individuals with anorexia nervosa (AN) often experience a range of additional psychiatric disorders. It would seem that some form of psychiatric comorbidity is the rule rather than the exception, reaching a prevalence rate as high as 97% (Blinder et al., 2006). Psychiatric comorbidity in adolescent AN patients was found to be less common than in adult samples, but being present at a rate of approximately 50% is still very meaningful (Bühren et al., 2014; McDermott et al., 2006; Salbach-Andrae et al., 2008), with depressive and anxiety disorders being the most prevalent comorbidities in the younger population (Fennig and Hadas, 2010; Salbach-Andrae et al., 2008).

There are relatively numerous publications on the rates of psychiatric comorbidities in AN, but studies on the effect of these comorbidities on the severity of AN are sparse. Many of those studies evaluated only the severity of subjective symptoms of an eating disorder (ED) in patients with AN with comorbid depressive and anxiety disorders (ANComorb) compared with patients with AN without comorbidity (ANNoComorb). The general findings were that the ANComorb patients reported having more severe subjective symptoms of EDs than the ANNoComorb patients, according to their responses to the subscales of the two main ED examinations/questionnaires, the Eating Disorders Examination (EDE) and the Eating Disorders Inventory–2 (EDI-2; Bizeul et al., 2003; McDermott et al., 2006; Milos et al., 2004; North and Gowers, 1999; Spindler and Milos, 2007). Only two studies (Bühren

et al., 2014; McDermott et al., 2006) compared objective measures between adolescent patients with ANComorb and ANNoComorb. Neither study demonstrated any group differences in body mass index (BMI) and amount of weight loss (Bühren et al., 2014; McDermott et al., 2006). The findings on the effect of duration of AN on the presence of comorbidities were mixed, with one study showing a longer history of AN illness in the comorbid group (McDermott et al., 2006) and another study showing no group difference in the length of illness duration (Bühren et al., 2014). The main limitations of the studies on the effect of comorbidity on AN severity were that many of them were conducted on adult AN patients although AN usually begins during adolescence. In addition, only two studies (Bühren et al., 2014; McDermott et al., 2006) used objective measures of AN severity (e.g., BMI, duration of illness and weight loss) and only one included measures of suicidality (Bühren et al., 2014).

Despite the high rate of coexisting depression and anxiety as well as the high rate of suicidality in adolescents with AN, the relationship between depression, anxiety, and suicidality in patients with AN has not been studied in depth. An earlier study by our group on a small sample of AN patients found that 24% of them had attempted suicide and that the risk for suicide attempt was associated with the level of depression (Fennig and Hadas, 2010).

The overall aim of the present study was to examine the potential effect of comorbid internalizing disorders on illness severity of ED in a sample of female adolescents diagnosed as having AN. Specifically, we compared selected objective and subjective measures among adolescent girls with ANComorb with those with ANNoComorb. We hypothesized that the ANComorb group would have a more severe disease course than the ANNoComorb group, as expressed by more severe symptoms, lowest ever BMI, earlier age of onset of illness, longer duration of illness, greater number of hospitalizations, and greater number of suicide attempts.

METHODS

Participants

Adolescent girls ($N = 88$) with a mean(SD) age of 15.94(2.19) years were enrolled through referrals from the inpatient and outpatient ED programs at the three major teaching hospitals affiliated with Tel Aviv University. They were evaluated as part of a multicenter, international collaborative study on the molecular genetics of AN. All study entrants met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)* criteria for AN. Because this was a genetic study, only participants of Jewish-Ashkenazi or Jewish-Sephardic descent were included. Exclusion criteria were a) nonpsychiatric diseases that could influence appetite, weight, or eating habits (such as diabetes); b) psychotic symptoms/disorder; c) mental retardation; and d) lack of adequate knowledge of Hebrew to respond to the questionnaires.

Seventy-nine subjects (89.8%) were recruited while they were at the acute stage, and nine (10.2%) were recruited while they were in remission. Sixty-nine subjects (78.4%) had AN restricting type, and 19 (21.6%) had AN bingeing/purging type. Forty-four subjects (50%) required inpatient hospitalization, 37 (42%) were attending a day hospitalization program, and 7 (8%) were receiving outpatient therapy.

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The study was reviewed and approved by the Research Ethics Committee (institutional review board) of each participating hospital. All participants received detailed information about the procedures and the aims of the study, and they and their parents signed a written consent form.

Measures

Lifetime histories of AN and additional *DSM-IV* disorders were assessed with the Hebrew version of the Structured Clinical Interview for Axis I *DSM-IV* Disorders—Patient Edition (Shalev et al., 1996). ED psychopathology was measured by the EDE (Cooper and Fairburn, 1987). The Cronbach's α for the total score was 0.89. Internal consistency values for the subscales were similar to those reported in similar publications, and they ranged from 0.53 to 0.76. The participants also completed the EDI-2 (Eberenz and Gleaves, 1994). The Hebrew translation was shown to have good internal consistency (0.67–0.93; Niv et al., 1998), and the Cronbach's α values were similar (0.63–0.92). We also reviewed the patients' medical records to collect information on the lowest ever BMI, age at AN onset, duration of illness (in months) before presentation, number of previous hospitalizations, and number of suicide attempts.

Procedure

The participants were interviewed individually at the hospital. All interviews were conducted face-to-face by a doctoral-level psychologist who had diagnostic assessment experience and had also undergone training on the administration of the various test instruments. The axis I diagnosis of AN and the presence of comorbid disorders were confirmed by consultation with a senior child and adolescent psychiatrist. Not all subjects completed all the assessments. The sample size is reflected in the *df* reported in the results.

Statistical Analysis

All statistical analyses were performed using the SPSS for Windows, 11.0. Data were analyzed by means of descriptive procedures, the chi-square test, analysis of variance, and multivariate analysis of variance. All tests were two tailed, with statistical significance set at the 0.05 probability level.

RESULTS

Diagnostic Groups

The subjects were divided into two groups. The ANnoComorb group was composed of 41 subjects (47%), and the ANComorb group was composed of 47 subjects (53%). The psychiatric comorbidities in the ANComorb group are listed in Table 1. There was no comorbid substance abuse disorder in our sample. Twenty-four subjects (27.3%) met the criteria for both depressive and anxiety disorders. The ANComorb and ANnoComorb groups were similar in mean (SD) age (16.15[2.53]years vs. 15.77[1.86]years, respectively; $t[174] = 1.13$, $p = 0.33$), ethnic distribution, and mean (SD) parent education years (9.93[2.13] vs. 9.70[1.64], respectively; $t[174] = 0.80$, $p = 0.29$). They were also similar in AN type, that is, restrictive versus bingeing/purging (Table 2).

Comparison Between AN With Comorbidity and AN Without Comorbidity

Objective Measures

The ANComorb group reported a significantly greater number of previous hospitalizations ($p = 0.001$) and significantly more suicide attempts than the ANnoComorb group ($p < 0.0001$; Table 2). There were no significant group differences in age at AN onset, duration of ED symptoms, and lowest ever BMI (Table 2).

TABLE 1. Prevalence of Coexisting Depressive and Anxiety Disorders in Adolescents With AN ($N = 88$)

Disorder Category	Subtype	<i>n</i> (%)
Depressive	Major depressive disorder	29 (33.0)
	Depressive disorder NOS	5 (5.7)
	Dysthymic disorder	9 (10.2)
Anxiety	Obsessive-compulsive disorder	14 (15.9)
	Social anxiety disorder	2 (2.3)
	Specific phobia	2 (2.3)
	Posttraumatic stress disorder	1 (1.1)
	Panic disorder	1 (1.1)
	Separation anxiety disorder	2 (2.3)
	More than one anxiety disorder	6 (6.8)

NOS indicates not otherwise specified.

Subjective Measures

The ANComorb patients reported significantly higher scores on all four EDE subscales (dietary restraints, concerns about eating, body shape, and weight) and a significantly higher total EDE score compared with the ANnoComorb patients ($p = 0.001$). In addition, the ANComorb patients reported significantly higher scores than the ANnoComorb subjects on 10 of the 11 EDI-2 subscales (drive for thinness, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse control, and social insecurity), with bulimia being the sole exception.

DISCUSSION

In this study, we focused on the impact of comorbid depression and anxiety disorders on the severity of ED in female adolescents with AN. As we had hypothesized, our findings indicated that the ANComorb group had significantly higher values in the subjective measures encompassing all EDE subscale scores and in 10 of the 11 EDI-2 subscale scores compared with the ANnoComorb group. This is in contrast to the few group differences in objective measures: specifically, the ANComorb group had a higher number of hospitalizations and a higher number of suicide attempts compared with the ANnoComorb group, whereas they did not differ in age at AN onset, duration of ED symptoms, and lowest ever BMI.

Surprisingly, few studies have investigated the effect of comorbidity on adolescents with AN although comorbid anxiety and depressive disorders are very common among individuals with AN (Bühren et al., 2014; McDermott et al., 2006; North and Gowers, 1999; Salbach-Andrae et al., 2008). Only one study investigated both subjective and objective measures of comorbidity in the adolescent population (McDermott et al., 2006). Those authors, however, did not use structured psychiatric evaluations in diagnosing the psychiatric comorbidities; used only a single diagnostic tool, the EDE interview, to evaluate severity of ED symptoms; and did not report on suicidality. Thus, to our knowledge, our current study is the most comprehensive report to date on the effect of psychiatric comorbidity on the subjective and objective clinical characteristics in adolescents with AN.

A robust finding of our study is the more severe level of almost all the psychological symptoms as assessed by the EDE and the EDI-2 in the ANComorb patients compared with the ANnoComorb patients, which is in line with previous studies (Bizeul et al., 2003; McDermott et al., 2006; Milos et al., 2004). Some of the symptoms identified by the EDI-2, such as feeling ineffective, perfectionism, and social insecurity, may be typical for both AN as well as anxiety and depression. These shared psychological traits could represent common endophenotypes

TABLE 2. Comparisons of ED Characteristics and Symptoms in AN Adolescents (*N* = 88) With and Without Comorbidities

Variable	Without Comorbidity	With Comorbidity	Statistics
Type of AN, <i>n</i> (%)			
Restrictive	35 (85.4)	34 (72.3)	$\chi^2_1 = 2.19, p = 0.14$
Bingeing/purging	6 (14.6)	13 (27.7)	
Age at AN onset, mean (SD), yrs	15.0 (2.8)	15.4 (1.6)	$t(86) = -1.00, p = 0.32$
Duration of symptoms, mean (SD), mos	17.5 (19.0)	19.2 (13.6)	$t(86) = -0.49, p = 0.63$
Lowest ever BMI, mean (SD), kg/m ²	14.50 (1.67)	15.10 (1.91)	$t(86) = -1.50, p = 0.14$
No. previous hospitalizations, mean (SD)	0.50 (0.75)	1.11 (0.95)	$t(86) = -3.31, p = 0.001$
Suicide attempts, <i>n</i> (%)			
None	41 (100.0)	34 (72.3)	$\chi^2_{1,87} = 13.31, p < 0.0001$
≥1	—	13 (27.7)	
EDE, mean (SD)			
Restraint	4.26 (1.51)	5.17 (0.73)	$F(1,71) = 10.84, p = 0.003$
Eating concern	2.45 (1.41)	3.38 (1.37)	$F(1,71) = 8.02, p = 0.012$
Shape concern	3.61 (1.50)	4.76 (1.24)	$F(1,71) = 12.8, p = 0.001$
Weight concern	3.6 (1.64)	4.48 (1.33)	$F(1,71) = 6.41, p = 0.027$
Total score	3.48 (1.30)	4.45 (0.95)	$F(1,71) = 13.14, p = 0.001$
EDI-2			
Drive for thinness	9.41 (5.85)	15.28 (4.9)	$F(1,67) = 20.26, p < 0.0001$
Bulimia	1.81 (4.12)	2.08 (2.88)	$F(1,67) = 0.10, p = 0.75$
Body dissatisfaction	11.19 (8.27)	18.14 (7.74)	$F(1,67) = 12.82, p = 0.001$
Ineffectiveness	6.03 (7.27)	13.22 (8.16)	$F(1,67) = 14.57, p = 0.0006$
Perfectionism	6.00 (4.29)	8.11 (3.80)	$F(1,67) = 4.63, p = 0.035$
Interpersonal distrust	3.66 (3.47)	5.81 (3.72)	$F(1,67) = 6.03, p = 0.03$
Introceptive awareness	5.41 (4.06)	11.83 (5.73)	$F(1,67) = 27.85, p < 0.0001$
Maturity fears	5.53 (5.10)	9.36 (5.49)	$F(1,67) = 8.82, p = 0.008$
Asceticism	4.50 (3.46)	7.89 (4.96)	$F(1,67) = 10.44, p = 0.004$
Impulse control	3.34 (4.33)	8.31 (6.27)	$F(1,67) = 14.07, p = 0.0007$
Social insecurity	4.00 (5.14)	7.11 (4.40)	$F(1,67) = 7.23, p = 0.009$

resulting from a common genetic diathesis to AN as well as anxiety and depression or common pathways related to shared environmental factors, for example, family relationships (Duclos et al., 2014; Keel et al., 2005; Wade et al., 2000). Other symptoms identified by the EDE such as dietary restraint and eating as well as body shape and weight concerns are more relevant in the context of AN than anxiety disorders and depression, suggesting that the presence of anxiety and depressive symptoms increases the level of severity of AN symptoms. In support of this possibility, it has been suggested that anxiety and depressive symptoms perpetuate AN symptoms (Spindler and Milos, 2007). For example, an anxious patient may more frequently engage in bingeing to counter negative emotions, and patients with AN and the comorbidity of depression are more likely to experience social difficulties and social isolation and therefore have fewer social “buffers” against ED-related behaviors (Spindler and Milos, 2007). Finally, the more severe symptoms in the ANComorb group compared with the ANnoComorb group may represent a nonspecific “dosage” effect of having multiple debilitating disorders versus having a single disorder.

Another important finding of our study is the higher rates of suicide attempts in the ANComorb group compared with the ANnoComorb group. Little is known about the AN patients at risk for committing suicide despite the facts that suicide is the second most common cause of death in AN (Sullivan, 1995) and that young suicide attempters are apparently at a higher risk for completed suicide later in life (Borst et al., 1991). Our finding supports previous reports of a high risk for suicidality associated with comorbidities of depression and anxiety in adolescents with EDs (Fennig and Hadas, 2010; Stein et al., 2004). The higher risk

for suicide attempts in our ANComorb group compared with our ANnoComorb group may also explain, at least in part, the higher number of hospitalizations in the former compared with the latter. Taken together, the more severe psychological symptoms, the higher suicidality risk, and the higher number of hospitalizations characterize ANComorb as being a more severe form of AN.

Surprisingly, there were no group differences in lowest ever BMI or in illness duration. The BMI findings are in agreement with a study by Bühren et al. (2014), who showed that ANComorb patients and ANnoComorb patients had similar BMIs and similar amounts of weight loss. It is possible that, because the anxiety and depressive symptoms are experienced as egodystonic and are characterized by feelings of suffering (in contrast to the egosyntonic nature of AN symptoms), they may motivate the AN patient to seek treatment. The greater likelihood for ANComorb patients to seek treatment is also indicated by the higher number of previous hospitalizations among them compared with the ANnoComorb patients. Inpatient treatments may protect these AN adolescents from a putatively greater decline in BMI, which most likely would have taken place had they not received treatment.

Our study has several limitations that should be noted. We included subjects with AN restrictive and AN bingeing/purging subtypes. These two subgroups may differ in terms of comorbidity and severity of illness, as suggested by previous studies (Bizeul et al., 2003; Salbach-Andrae et al., 2008). To verify that our results had not been biased by one of these AN subtypes, we repeated the analyses of AN restrictive and AN bingeing/purging subtypes separately and received similar results to the analyses conducted for the group as a whole. Another

limitation is the cross-sectional design of the study, which prevented us from drawing definite conclusions on cause and effect relations between AN and having a comorbidity of anxiety and depressive disorders. Lastly, the clinical data were self-reported by the patients and their families, and accuracy was subject to recall and other biases.

In conclusion, our findings suggest that ANComorb is a more severe clinical variant of the disorder, especially with respect to psychological symptoms and suicide risk. In addition to more intense case management and antidepressant medications, ANComorb patients' treatment should focus on the common psychological symptoms present in this group, such as interpersonal mistrust and ineffectiveness, perfectionism, social insecurity, as well as low self-esteem. Additional studies are recommended to explore whether cognitive-behavioral and interpersonal therapies that focus on alleviating these symptoms will be effective in treating ANComorb patients.

DISCLOSURES

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REFERENCES

- Bizeul C, Brun JM, Rigaud D (2003) Depression influences the EDI scores in anorexia nervosa patients. *Eur Psychiatry*. 18:119–123.
- Blinder BJ, Cumella EJ, Sanathara VA (2006) Psychiatric comorbidities of female inpatients with eating disorders. *Psychosom Med*. 68:454–462.
- Borst SR, Noam GG, Bartok JA (1991) Adolescent suicidality: A clinical-developmental approach. *J Am Acad Child Adolesc Psychiatry*. 30:796–803.
- Bühren K, Schwarte R, Fluck F, Timmesfeld N, Krei M, Egberts K, Pfeiffer E, Fleischhaker C, Wewetzer C, Herpertz-Dahlmann B (2014) Comorbid psychiatric disorders in female adolescents with first-onset anorexia nervosa. *Eur Eat Disord Rev*. 22:39–44.
- Cooper Z, Fairburn C (1987) The eating disorder examination: A semi-structured interview for the assessment of the specific psychopathology of eating disorders. *Int J Eat Disord*. 6:1–8.
- Duclos J, Dorard G, Berthoz S, Curt F, Faucher S, Falissard B, Godart N (2014) Expressed emotion in anorexia nervosa: What is inside the “black box”? *Compr Psychiatry*. 55:71–79.
- Eberenz KP, Gleaves DH (1994) An examination of the internal consistency and factor structure of the eating disorder inventory-2 in a clinical sample. *Int J Eat Disord*. 16:371–379.
- Fennig S, Hadas A (2010) Suicidal behavior and depression in adolescents with eating disorders. *Nord J Psychiatry*. 64:32–39.
- Keel PK, Klump KL, Miller KB, McGue M, Iacono WG (2005) Shared transmission of eating disorders and anxiety disorders. *Int J Eat Disord*. 38:99–105.
- McDermott B, Forbes D, Harris C, McCormack J, Gibbon P (2006) Non-eating disorders psychopathology in children and adolescents with eating disorders: Implications for malnutrition and symptom severity. *J Psychosom Res*. 60:257–261.
- Milos G, Spindler A, Schnyder U (2004) Psychiatric comorbidity and Eating Disorder Inventory (EDI) profiles in eating disorder patients. *Can J Psychiatry*. 49:179–184.
- Niv N, Kaplan Z, Mitrani E, Shiang J (1998) Validity study of the EDI-2 in Israeli population. *Isr J Psychiatry Relat Sci*. 35:287.
- North C, Gowers S (1999) Anorexia nervosa, psychopathology, and outcome. *Int J Eat Disord*. 26:386–391.
- Salbach-Andrae H, Lenz K, Simmendinger N, Klinkowski N, Lehmkühl U, Pfeiffer E (2008) Psychiatric comorbidities among female adolescents with anorexia nervosa. *Child Psychiatry Hum Dev*. 39:261–272.
- Shalev AY, Abramowitz MZ, Kaplan De Nour A (1996) *Structured Clinical Interview for Axis I DSM-IV Disorders—Patient Edition (SCID-I/P, Version 2.0) (Hebrew Version)*. Jerusalem: Hadassah University Hospital.
- Spindler A, Milos G (2007) Links between eating disorder symptom severity and psychiatric comorbidity. *Eat Behav*. 8:364–373.
- Stein D, Lilienfeld LR, Wildman PC, Marcus MD (2004) Attempted suicide and self-injury in patients diagnosed with eating disorders. *Compr Psychiatry*. 45:447–451.
- Sullivan PF (1995) Mortality in anorexia nervosa. *Am J Psychiatry*. 152:1073–1074.
- Wade TD, Bulik CM, Neale M, Kendler KS (2000) Anorexia nervosa and major depression: Shared genetic and environmental risk factors. *Am J Psychiatry*. 157:469–471.