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After studying this article, you should be able to:

- Integrate strategies focused on modifying risk factors for metabolic syndrome in the management of bipolar disorder in young patients

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High Prevalence of Metabolic Syndrome Among Adolescents and Young Adults With Bipolar Disorder

Christine Li, MD[a,b]; Boris Birmaher, MD[c]; Brian Rooks, PhD[c]; Mary Kay Gill, MSN, JD[c]; Heather Hower, MSW[d]; David A. Axelson, MD[e]; Daniel P. Dickstein, MD[d,f]; Tina R. Goldstein, PhD[c]; Fangzi Liao, MS[c]; Shirley Yen, PhD[d,g,j]; Jeffrey Hunt, MD[d,f]; Satish Iyengar, PhD[h]; Neal D. Ryan, MD[c]; Michael A. Strober, PhD[i]; Martin B. Keller, MD[g]; and Benjamin I. Goldstein, MD, PhD[a,b,*]

ABSTRACT

Objective: Despite abundant literature demonstrating increased metabolic syndrome (MetS) prevalence and important clinical correlates of MetS among middle-age adults with bipolar disorder, little is known about this topic among adolescents and young adults early in their course of bipolar disorder. We therefore examined this topic in the Course and Outcome of Bipolar Youth (COBY) study.

Methods: A cross-sectional, retrospective study was conducted of 162 adolescents and young adults (mean ± SD age = 20.8 ± 3.7 years; range, 13.6–28.3 years) with bipolar disorder (I, II, or not otherwise specified, based on *DSM-IV*) enrolled in COBY between 2000 and 2006. MetS measures (blood pressure, glucose, high-density lipoprotein cholesterol [HDL-C], triglycerides, and waist circumference), defined using the International Diabetes Federation criteria, were obtained at a single timepoint. Mood, comorbidity, and treatment over the 6 months preceding the MetS assessment were evaluated using the Longitudinal Interval Follow-Up Evaluation.

Results: The prevalence of MetS in the sample was 19.8% (32/162). Low HDL-C (56.5%) and abdominal obesity (46.9%) were the most common MetS criteria. MetS was nominally associated with lower lifetime global functioning at COBY intake (odds ratio [OR] = 0.97, $P = .06$). MetS was significantly associated with percentage of weeks in full-threshold pure depression (OR = 1.07, $P = .02$) and percentage of weeks receiving antidepressant medications (OR = 1.06, $P = .001$) in the preceding 6 months. MetS was not associated with manic symptoms or medications other than antidepressants.

Conclusions: The prevalence of MetS in this sample was at least double compared to the general population. Moreover, MetS is associated with increased burden of depression symptoms in this group. Management of early-onset bipolar disorder should integrate strategies focused on modifying MetS risk factors.

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Clinical Points

- Despite greatly increased cardiovascular risk in bipolar disorder, few studies have examined this topic early in life.
- There are increased rates of metabolic syndrome, a clustering of cardiovascular risk factors, in adolescents and young adults with bipolar disorder, especially those with more persistent depression.
- Improvements in cardiovascular health or depression may have reciprocal benefits for patients.

[a]Centre for Youth Bipolar Disorder, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

[b]University of Toronto Faculty of Medicine, Toronto, Ontario, Canada

[c]Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

[d]Department of Psychiatry and Human Behavior, Warren Alpert Medical School of Brown University, Providence, Rhode Island

[e]Department of Psychiatry, Nationwide Children's Hospital and The Ohio State College of Medicine, Columbus, Ohio

[f]Bradley Hospital, Riverside, Rhode Island

[g]Butler Hospital, Riverside, Rhode Island

[h]Department of Statistics, University of Pittsburgh, Pittsburgh, Pennsylvania

[i]Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, UCLA, Los Angeles, California

[j]Massachusetts Mental Health Center and Department of Psychiatry, Beth Israel Deaconess Medical Center, Boston, Massachusetts (current affiliations)

*Corresponding author: Benjamin I. Goldstein, MD, PhD, Centre for Youth Bipolar Disorder, Sunnybrook Health Sciences Centre, 2075 Bayview Ave, EG-48, Toronto, Ontario, Canada (benjamin.goldstein@sunnybrook.ca).

Bipolar disorder (BD) is a recurrent and severe mood disorder that, in addition to the burden of depressive and manic symptoms, is associated with significant medical and psychiatric comorbidities.[1] Numerous studies have demonstrated a high prevalence of metabolic syndrome (MetS) and MetS components (obesity, dyslipidemia, hypertension, and hyperglycemia) in adults with BD,[2–9] with MetS prevalence ranging from about 10% to over 60%.[2,10] MetS is a cluster of clinical and biochemical abnormalities that predispose individuals to cardiovascular disease (CVD) and diabetes mellitus.[11] The International Diabetes Federation (IDF) criteria for MetS require the presence of central obesity (waist circumference > 37 in for men, > 31.5 in for women) plus any 2 of high triglycerides (≥ 150 mg/dL), low high-density lipoprotein cholesterol (HDL-C; < 40 mg/dL for men, < 50 mg/dL for women), high systolic (> 130 mm Hg) and/or diastolic (> 85 mm Hg) blood pressure, and high fasting glucose (≥ 100 mg/dL).[12] A meta-analysis of 81 articles, including 6,983 adult participants, found 37.3% prevalence of MetS in BD, an odds ratio of 1.97 versus the general population, and increased risk of MetS among those currently treated with antipsychotics.[10] Among individual MetS components, abdominal obesity is the most common criterion (48.7%–61% depending on the specific MetS definition), followed by high blood pressure (47.1%), low HDL-C (42.1%), and high triglycerides (39.3%), with high glucose being the least common (11.4%–17.3%, depending on the specific MetS definition).

CVD is a leading cause of increased mortality in individuals with BD.[13] The presence of MetS and its components is associated with increasing age[4,14–18] as well as with important clinical characteristics among adults with BD including antipsychotic medications,[19–21] more psychiatric hospitalizations,[22] and suicide attempts.[23] Specific MetS components such as obesity have also been linked with proxies for greater BD severity including poorer treatment outcome,[24] rapid cycling, chronic course,[25] and lower functioning.[22,25] Although most clinical studies include patients taking medications with known propensity for MetS criteria (eg, antipsychotics, lithium, divalproex), particularly obesity, epidemiologic studies that include BD samples with low rates of antimanic medication use have also reported increased rates of obesity in BD.[26,27]

Despite the substantial number of studies investigating MetS in adults with BD,[2] little is known about MetS among adolescents and young adults with BD. One study of 200 Italian adults with BD included 22 subjects between the ages of 18 and 30 years. The prevalence of MetS was 9.1% in this age group, and the rate increased linearly with age.[28] This value is higher than the MetS prevalence of 4.2% in the general pediatric and adolescent population in southern Italy.[29] Other studies have investigated specific components of MetS[30–33] or focused on the effects of antipsychotics on dimensional levels of MetS criteria (eg, changes in triglyceride levels) among youth with BD.[34,35] For example, a study of 1,841 pediatric BD patients found that the BD cohort had increased rates of obesity and diabetes mellitus compared to healthy controls and that these higher rates are associated with more outpatient service use.[31] Data from the Course and Outcome of Bipolar Illness in Youth (COBY) study revealed a 42% prevalence of overweight and obesity among pediatric BD subjects compared to 34% among the general youth population.[30] Being overweight or obese was found to be most robustly associated with younger age, nonwhite race, lifetime physical abuse, substance use disorders, psychiatric hospitalizations, and exposure to ≥ 2 medication classes associated with weight gain.[30] Another study of 1,848 BD subjects in Taiwan reported higher prevalence and incidence of hypertension in young adults with BD compared to the general population.[33]

Considering the findings of increased MetS prevalence and important clinical correlates of MetS among primarily middle-aged adults with BD, additional studies on MetS among youth and young adults with BD are indicated. The only prior study regarding MetS in this age range had a small number of subjects (N = 22),[28] precluding an examination of clinical correlates. MetS confers significant risk for CVD, and the risk ratio for CVD mortality in BD compared to the general population is highest among young adults.[36,37] For example, a study examining CVD mortality in Sweden reported that the CVD mortality rate ratios among BD patients between 25–34 years old is about 8, compared

to 2 to 4 among older BD patients.[36] Indeed, BD among adolescents was recently highlighted by the American Heart Association as a moderate-risk condition associated with accelerated atherosclerosis and early CVD.[38] We therefore examined the prevalence of MetS and its components, as well as their clinical correlates, in a relatively large sample of adolescents and young adults with BD enrolled in the COBY study. We hypothesized that the prevalence of MetS in COBY would be greater than the general population and that MetS would be associated with exposure to antimanic medications, greater mood symptom burden, higher rates of suicide attempts and hospitalizations, and lower global functioning.

METHODS

Metabolic Syndrome

Metabolic syndrome was defined using the International Diabetes Federation (IDF) criteria,[39] requiring the presence of central obesity (waist circumference >37 in for men, >31.5 in for women), plus any 2 of high triglycerides (≥150 mg/dL), low HDL-C (<40 mg/dL for men, <50 mg/dL for women), high systolic (>130 mm Hg) and/or diastolic (>85 mm Hg) blood pressure, and high fasting glucose (≥100 mg/dL). Waist circumference was measured with a SECA 201 girth measuring tape according to IDF guidelines.[40] For subjects under the age of 16, waist circumference percentile values from IDF were used.[39] Blood was drawn from each subject between 9:00 AM–12:00 PM after a 10-hour fast and sent to the local hospital laboratory for analysis of glucose and lipids levels. Systolic and diastolic blood pressure was measured twice using Life Source automated blood pressure monitors, with analyses examining the mean measurements.

Participants

The methods for COBY have been described in detail elsewhere.[41–43] In short, the study involved youths ages 7 to 17 years 11 months at intake, with *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*) BD I or II or operationally defined BD not otherwise specified (NOS). Participants in the present cross-sectional, retrospective analysis included 162 adolescents and young adults, with a mean ± SD age of 20.8 ± 3.7 years (range, 13.6–28.3 years), 40.7% females, and 81.5% white race (similar to 45.5% females and 82.6% white race in the overall COBY sample), enrolled in COBY with BD I (69.1%), II (14.8%), or NOS (16%). Consecutive participants contacted for follow-up visits as part of the overall COBY study at the Pittsburgh and Brown sites were invited to participate. Participants completed a MetS visit 8.52 ± 1.60 years after enrollment in COBY. Participants are being followed prospectively, and future longitudinal studies will be forthcoming. Exclusion criteria were infectious illness within 14 days, known inflammatory or autoimmune illness, use of steroidal medication or insulin within 1 month of the MetS visit, self-reported alcohol or illicit drug use within 24 hours, and pregnancy.

Procedures

Each participating university's institutional review board approved the study. At enrollment, participants and parents gave informed consent and were directly interviewed for the presence of current and lifetime psychiatric illnesses in the youths.

Psychiatric and Anthropometric Measures

Psychiatric diagnoses were validated with the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL),[44] the Kiddie Mania Rating Scale,[45] and the depression section of the K-SADS-P.[46] Psychiatric symptoms over the 6-month period preceding the MetS visit were evaluated using the Longitudinal Interval Follow-Up Evaluation (LIFE)[47] and tracked on a week-by-week basis using this instrument's Psychiatric Status Rating (PSR) scales. Analyses focused on PSR scores over the 6 months prior to the measurement of MetS components, as this was the target interval between COBY visits and associations between MetS and its predictors were anticipated to be strongest when examining the most proximal epoch of follow-up.

All assessments were performed by research staff trained to reliably administer the interviews. Interview results were presented to child psychiatrists or psychologists, who confirmed the diagnoses and PSR scores. κ values for psychiatric disorders on the K-SADS were ≥0.8, and intraclass correlation coefficients for syndromal/subsyndromal mood symptoms via the PSR were ≥0.75.

First- and second-degree family psychiatric history was ascertained using the Family History Screen.[48] Socioeconomic status was ascertained at intake using the 4-factor Hollingshead scale.[49] Abuse was ascertained using the KSADS-PL. Current and lifetime pharmacologic treatment exposure were obtained at the intake assessment. In addition, the Psychotropic Treatment Record and the Psychosocial Treatment Schedule of the LIFE were used to ascertain treatment exposure in the preceding 6-month period on a week-by-week basis. Weekly exposure was dichotomized (yes/no) for any psychotropic medication and for each of the following: antimanic anticonvulsants (ie, carbamazepine and/or divalproex sodium), lithium, second-generation antipsychotics, antidepressants, and stimulants. Weekly exposure to psychosocial treatments was likewise examined for 3 categories of intensity: inpatient hospitalization/residential treatment, specialized intensive services, and standard outpatient services. Global functioning was assessed at intake using the Children's Global Assessment Scale (C-GAS).[50]

Statistical Analyses

Statistical analyses were performed using SAS (9.3) software. Correlations among the MetS components were examined with Pearson correlation coefficients. Comparisons of demographic and lifetime clinical characteristics by MetS group were performed using parametric and nonparametric tests where appropriate.

Table 1. Demographic, Clinical, and Family Psychiatric History Correlates of Metabolic Syndrome Among Adolescents and Young Adults With Bipolar Disorder[a]

	MetS Group				
	MetS Absent (n = 130)	MetS Present (n = 32)	Wald χ^2	Odds Ratio	*P* Value
Demographics					
Age, mean (SD), y	20.67 (3.8)	20.90 (3.7)	0.31		.76
Race, white	108 (83.1)	24 (75.0)	1.11		.29
Sex, female	53 (40.8)	13 (40.6)	0.00		.99
Lifetime clinical history					
ADHD	97 (74.6)	26 (81.3)	0.61	1.47	.43
Anxiety	89 (68.5)	23 (71.9)	0.14	1.18	.71
Conduct disorder	36 (27.7)	8 (25.0)	0.09	0.87	.76
Oppositional defiant disorder	76 (58.5)	22 (68.8)	1.13	1.56	.29
Substance use disorder	43 (33.1)	11 (34.4)	0.02	1.06	.89
Psychosis	51 (39.2)	10 (31.3)	0.69	0.70	.40
Psychiatric hospitalization	82 (63.1)	23 (71.9)	0.86	1.50	.35
Suicide attempt	60 (46.2)	19 (59.4)	1.77	1.71	.18
Self-injurious behavior	77 (59.2)	16 (50.0)	0.89	0.69	.35
Suicidal ideation	104 (80.0)	26 (81.3)	0.03	1.08	.87
Physical abuse	22 (16.9)	6 (18.8)	0.06	1.13	.81
Sexual abuse	16 (12.3)	6 (18.8)	0.89	1.64	.34
Most severe lifetime C-GAS score (at study intake), mean (SD)	39.11 (10.8)	34.80 (12.1)	3.58	0.97	.06
Family psychiatric history (1st and 2nd degree)					
Depression	120 (92.3)	28 (87.5)	0.74	0.58	.39
Mania/hypomania	88 (67.7)	21 (65.6)	0.05	0.91	.82
ADHD	71 (54.6)	17 (53.1)	0.02	0.94	.88
Anxiety	103 (79.2)	23 (71.9)	0.80	0.67	.37
Conduct disorder	50 (38.5)	14 (43.8)	0.30	1.24	.58
Schizophrenia	15 (11.5)	1 (3.1)	1.76	0.25	.18
Substance use disorder	100 (76.9)	23 (71.9)	0.36	0.77	.55
Suicide attempt or completion	64 (49.2)	18 (56.3)	0.50	1.33	.48
Lifetime psychiatric medications					
Any psychotropic medication	70 (54.3)	23 (71.9)	3.26		.07
Antimanic anticonvulsants	8 (6.2)	4 (12.5)	1.47		.22
Lithium	13 (10.1)	5 (15.6)	0.79		.37
Second-generation antipsychotics	45 (34.6)	14 (43.8)	0.93		.34
Antidepressants	24 (18.6)	16 (50.0)	13.53		.0002
Stimulants	29 (22.5)	9 (28.1)	0.45		.50

[a]Values expressed as n (%) unless otherwise noted.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, C-GAS = Children's Global Assessment Scale, MetS = metabolic syndrome.

Logistic regression models were used to analyze the associations between presence of MetS and prospective course variables collected during the 6 months preceding blood draw. The percentages of weeks with sub- and full-threshold criteria for depression, mania/hypomania, and comorbid conditions were converted to number of weeks with sub- and full-threshold criteria, respectively, giving an associated odds ratio that reflects the expected percent increase in odds of having MetS for an additional week of symptoms. Demographic and/or lifetime clinical measures that exhibited significant associations with presence of MetS at the $P \leq .10$ level were included in multiple logistic regression models as potential confounders. Given the hypothesis-generating (ie, exploratory) nature of the current study, we did not correct for multiple comparisons.

RESULTS

The overall prevalence of MetS in the sample was 19.8% (32/162). The prevalence of each MetS criterion was as follows: low HDL-C: 56.5%, abdominal obesity: 46.9%, high blood pressure: 24.2%, high triglycerides: 15.4%, and high glucose: 15.4%. The proportion of participants with varying counts of MetS components was as follows: 21.3% for 0 MetS components, 30% for 1 component, 28.1% for 2 components, and 20.6% for 3+ components; 78.8% of participants had at least 1 MetS component, while 48.8% had at least 2. The mean waist circumference was 35.3 inches (SD = 5.6; range, 23.8–56.8). The mean systolic blood pressure was 115.30 mm Hg (SD = 10.67; range, 90.0–142.5), and mean diastolic blood pressure was 77.09 mm Hg (SD = 9.54; range, 47.5–104.5). The mean triglyceride level was 100.68 mg/dL (SD = 79.4; range, 25.0–636.0). The mean glucose level was 93.17 mg/dL (SD = 14.93; range, 56.0–239.0). The mean HDL-C was 47.56 mg/dL (SD = 15.95; range, 21.0–101.0). We examined the co-occurrence of MetS components pairwise among participants with MetS. The most common co-occurrences were central obesity with low HDL-C (96.8%), central obesity with high diastolic blood pressure (51.6%), and low HDL-C with high diastolic blood pressure (50.0%).

For comparative reasons, we also examined MetS using the National Cholesterol Education Program (NCEP) definitions. The NCEP criteria are identical to the IDF criteria, except abdominal obesity is defined as waist

Table 2. Association of Metabolic Syndrome With Psychiatric Symptoms and Treatment in the Preceding 6 Months

Psychiatric Symptoms	Odds Ratio[a]	95% Confidence Interval	Unadjusted *P* Value	Adjusted *P* Value
Maximum symptom severity in preceding 6 months				
Depression	1.19	0.92–1.53	.18	.35
Mania/hypomania	0.96	0.75–1.24	.77	.85
Psychosis	1.01	0.95–1.07	.81	.79
Percentage of weeks with symptoms in preceding 6 months				
No significant mood symptoms	0.98	0.95–1.02	.39	.43
Any subthreshold mood state	0.98	0.94–1.02	.34	.38
Any full-threshold mood state	1.05	1.00–1.10	.04	.07
Full-threshold pure depression	1.07	1.01–1.13	.02	.04
Full-threshold pure mania/hypomania	1.00	0.89–1.13	.97	.91
Full-threshold mixed state	0.82	0.33–2.02	.67	.69
Suicidal ideation	1.08	0.99–1.19	.09	.11
Any comorbid disorder	1.00	0.97–1.04	.84	.91
ADHD	1.00	0.97–1.03	.81	.99
Any anxiety	1.02	0.99–1.05	.21	.16
CD/ODD	1.01	0.98–1.04	.56	.75
Substance use disorder[d]	0.99	0.96–1.03	.81	.76
Percentage of weeks with psychiatric treatment in preceding 6 months				
Any psychosocial	0.99	0.94–1.04	.65	.44
Inpatient/residential treatment	0.68	0.29–1.60	.38	.39
Specialized psychosocial services	0.97	0.89–1.05	.43	.36
Outpatient services	1.02	0.96–1.08	.63	.83
Any psychotropic medication	1.03	0.99–1.07	.07	.21
Antimanic anticonvulsants	1.04	0.99–1.10	.12	.20
Lithium	1.02	0.98–1.06	.37	.50
Second-generation antipsychotics	1.02	0.99–1.05	.3	.64
Antidepressants	1.06	1.02–1.10	.001	.001
Stimulants	1.01	0.98–1.05	.5	.99

[a]Unit of interpretation for odds ratio is 1 week.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, CD/ODD = conduct disorder/oppositional defiant disorder.

circumference > 40 inches for men and > 35 inches for women, and MetS requires any 3 of central obesity, high triglycerides, low HDL-C, high systolic and/or diastolic blood pressure, and high fasting glucose.[51] Using the NCEP criteria, the prevalence of MetS is 16.1% (26/162), compared to 19.8% using the IDF criteria. The prevalence of MetS components using the NCEP criteria are identical to those using IDF criteria, except the prevalence of abdominal obesity (30.4%) is lower than that of IDF criteria (46.9%).

Table 1 presents the demographic, clinical, and family psychiatric history correlates of MetS. There was only a nonsignificant association (OR = 0.97, $P = .06$) between most severe lifetime C-GAS rating at intake and presence of MetS; this variable was therefore included as a covariate for subsequent analyses. We also evaluated in exploratory fashion whether atypical depression symptoms were associated with MetS. Because the PSR scale does not rate the severity of individual symptoms, we addressed this topic based on the presence of the following atypical depression symptoms from the K-SADS-P depression section at intake: increased sleep, fatigue, increased weight and/or appetite. Participants with, as compared to without, MetS were nominally more likely to have had increased sleep (28.1% vs 12.4%, $P = .05$) and nominally more likely to have all 3 of the atypical depression symptoms (12.5% vs 3.1%, $P = .05$).

Table 2 presents the association between predictors of MetS in the 6 months preceding assessment of MetS. Presence of MetS was significantly associated with percentage of weeks in any full-threshold mood state (OR = 1.05, $P = .04$, 95% CI = 1.00–1.10), percentage of weeks in full-threshold pure depression (OR = 1.07, $P = .02$, 95% CI = 1.01–1.13), and percentage of weeks receiving antidepressant medications (OR = 1.06, $P = .001$, 95% CI = 1.02–1.10) in univariate analyses. Only the associations with depression symptoms and antidepressants remained significant after controlling for most severe lifetime C-GAS at intake.

To address the issue of concomitant medications, we undertook 2 sensitivity analyses. We first reran the logistic regression while sequentially covarying for each additional medication class, and odds ratio estimate for antidepressant use was virtually unchanged in each model (1.06–1.07, P values < .003). We next reran the logistic regression after sequentially excluding subjects using each of the other medication classes, and again the odds ratio estimate for antidepressant use was virtually unchanged (1.06–1.07, P values ≤ .02).

DISCUSSION

To our knowledge, this is the first study to focus on MetS among adolescents and young adults with BD. The overall prevalence of MetS, using IDF criteria, in the current study sample was 19.8%. Abdominal obesity and low HDL-C were the most common, whereas high triglycerides and elevated glucose were the least common criteria. MetS was significantly associated with most severe lifetime C-GAS rating at intake. Contrary to hypotheses, antimanic medications, and second-generation antipsychotics specifically, were not significantly associated with MetS. However, the burden of overall depression symptoms and of

any full-threshold mood state over the preceding 6 months was greater, as was use of antidepressant medications, among participants with MetS. The prevalence of MetS in this sample was higher than the prevalence of 9.1% found among 22 young adults with BD in an Italian sample.[28] In contrast, the prevalence of MetS in this study was lower than those found in most adult BD samples, in which the prevalence of MetS can exceed 60% (defined using various criteria).[2,10] This finding is expected as MetS is generally less prevalent in youth and increases with age.[28,52] By comparison to the current sample, the prevalence of IDF-defined MetS among adolescents in the general US population is 5.5%.[53]

The study has 3 primary limitations that should be considered before interpreting the findings. First, this study is based on a single measurement of MetS components, which precludes conclusions regarding causality and/or direction of the observed associations. Repeated-measures analyses will be informative in better understanding the associations between MetS and mood symptoms in BD. Second, the study did not include a healthy and/or clinical control group. Thus, it is not clear whether the associations observed in the current study are specific to BD. However, it is important to note the prevalence of MetS in the current study is substantially higher than that reported in the comparably aged general population. Third, the study is based on a clinical sample and may not be representative of untreated adolescents and young adults with BD.

The prevalence of hypertriglyceridemia (15.4%) among BD participants was similar to US adolescents in the general population (14.2%).[53] BD participants had increased prevalence of abdominal obesity (46.9% vs 34.7%), low HDL-C (56.5% vs 21.6%), high blood pressure (24.2% vs 4.1%), and high glucose (15.4% vs 11.8%) compared to US adolescents in the general population. In addition, there was a greater proportion of participants with 3+ MetS components among BD adolescents (13.6% vs 5.5%), whereas the proportion with 2+ MetS components was similar (24.7% vs 21.3%).[53]

We found that the burden of depression and any full-threshold mood state symptoms in the preceding 6 months was greater among participants with MetS. Previous studies have reported associations between depression and higher prevalence of MetS.[54] Putative links between mood symptoms and MetS include the direct effect of those symptoms (eg, sleep disturbance, sedentary lifestyle, increased appetite), the effects of treatments targeting those symptoms (as described below), and shared biological mechanisms such as inflammation. Indeed, a recent study regarding inflammation based on the COBY sample found that several MetS components were associated with increased levels of proinflammatory markers.[43]

Although antidepressants have been associated with weight gain, there is less evidence that modern antidepressants confer meaningfully increased risk of MetS.[55–58] The maximum severity of depression symptoms in the preceding 6 months was not associated with MetS; however, it remains possible that this latter association is confounded by indication, whereby participants with more severe depression were more likely to receive antidepressant treatment. Indeed, among young adult women, history of major depression is associated with a 2-fold risk of MetS, independent of demographic characteristics, smoking, physical activity, nutrition, and alcohol use.[59] Similar associations are observed for self-reported depression symptoms.[60] Another recent study found that presence of major depression with anhedonia in a community sample of young adults is associated with increased prevalence of MetS, whereas this was not the case for major depression without anhedonia.[61] Future studies are warranted to evaluate for sex differences and for specific symptom-related differences in terms of the link between MetS and depression in youth and young adults.

In contrast to contemporary antidepressants, antimanic medications in general, and second-generation antipsychotics in particular, are consistently associated with increased prevalence of MetS and its components in adults with BD.[2,10] We previously reported that overweight/obesity among COBY participants at intake was associated with lifetime use of second-generation antipsychotics in univariate but not multivariate analyses.[30] One may speculate that there are developmental differences in terms of risk factors for MetS in BD; for example, the impact of psychiatric symptoms and shared biology on MetS may be greater in youth, whereas the impact of psychiatric medications on MetS is greater in adults. Replication studies are warranted to evaluate this and other putative explanations for the lack of association between antimanic medications and MetS. Similarly, although we did not replicate previous studies that demonstrated associations between MetS and psychiatric hospitalization[23] and suicide attempts,[3,62] present findings were in the same direction, with numerically greater prevalence of MetS among COBY participants with lifetime history of psychiatric hospitalization (OR = 1.50, $P = .35$) and suicide attempt (OR = 1.71, $P = .18$).

In summary, this is the first study to examine the prevalence of MetS and its components, as well as their clinical correlates, in a relatively large sample of adolescents and young adults with BD. This study revealed that the prevalence of MetS among youth with BD is roughly quadruple that of the general population and that MetS is associated with increased burden of depression symptoms. Although results in the current study require replication in other samples with a direct comparison group, our findings suggest that excessive rates of MetS and its components, which are risk factors for CVD and diabetes, are already apparent among adolescents and young adults with BD. This phenomenon calls for the need to implement early screening, prevention, and intervention strategies for MetS and its components. Management of BD should ideally integrate medical and psychiatric care with attention on modifying MetS risk factors.[63–65] Finally, the possibility that reducing MetS can reduce the burden of depression in BD remains, and studies addressing this topic are warranted.

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For the CME Posttest, see next page.

POSTTEST

To obtain credit, go to PSYCHIATRIST.COM **(Keyword: August CME) to take this Posttest and complete the Evaluation.** A $10 processing fee is required.

1. **Metabolic syndrome and its components have been associated with which of the following risk factors or risks?**
   a. Suicide attempts
   b. Antipsychotic medications
   c. Increasing age
   d. All of the above
2. **Jennifer is a 17-year-old girl with bipolar disorder and a family history of cardiovascular disease. You seek to evaluate Jennifer for metabolic syndrome and its components. Which metabolic syndrome criteria require the use of sex-specific benchmarks that you would want to employ with Jennifer?**
   a. Waist circumference, diastolic blood pressure
   b. Triglycerides, glucose
   c. Waist circumference, high-density lipoprotein cholesterol (HDL-C)
   d. There are no sex-specific benchmarks for metabolic syndrome criteria
3. **Which of the following statements *best* summarizes the results of the current study?**
   a. Metabolic syndrome was associated with the severity of manic symptoms and the use of antimanic medications
   b. Metabolic syndrome was associated with the severity of depressive symptoms and the use of antidepressant medications
   c. Metabolic syndrome was associated with the severity of depressive and manic symptoms and the use of antidepressant and antimanic medications
   d. Metabolic syndrome was not associated with mood symptom severity nor with specific classes of medications