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Associations between comorbid anxiety, diabetes control, and overall medical burden in a population with serious mental illness and diabetes

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Abstract

Objective—While previous work has demonstrated elevation of both comorbid anxiety disorders and diabetes mellitus type II (DM2) in individuals with Serious Mental Illness (SMI), little is known regarding the impact of comorbid anxiety on DM2 outcomes in SMI populations. We analyzed baseline data from a population of SMI patients with DM2 to study relationships between comorbid anxiety, glucose control as measured by HbA1c score, and overall illness burden.

Methods—Using baseline data from an ongoing prospective treatment study involving 157 individuals with SMI and DM2 we compared individuals with and without a comorbid anxiety disorder and compared HbA1c levels between these groups to assess the relationship between anxiety and management of DM2. We conducted a similar analysis using cumulative number of anxiety diagnoses as a proxy for anxiety load. Finally, we searched for associations between anxiety and overall medical illness burden as measured by Charlson score.

Results—Anxiety disorders were seen in 33.1 % (N= 52) of individuals with SMI and DM2 and were associated with increased severity of depressive symptoms and decreased function. HbA1c levels were not significantly different in those with or without anxiety and having multiple anxiety disorders was not associated with differences in DM2 control. However, depressive symptoms were significantly associated with higher HbA1c levels. Neither comorbid anxiety nor anxiety load were significantly associated with overall medical burden.

Conclusion—One in 3 people with SMI and DM2 have anxiety. Depressive symptoms were significantly associated with Hb1Ac levels while anxiety symptoms had no relation to HbA1c; this is consistent with previously published work. More studies are needed to better understand the relationship between depression, anxiety and health management in people with SMI and DM2.

Keywords

Serious mental illness; schizophrenia; bipolar disorder; anxiety; Diabetes mellitus; comorbidity

Introduction

The prevalence of comorbid anxiety disorders is known to be higher among patients with serious mental illness (SMI) than the general population.[1-7] Whatever the specific anxiety diagnosis or etiology, evidence supports elevated psychotic and depressive symptoms, as well as decreased psychosocial function, in SMI patients with comorbid anxiety versus those without.[2, 3, 5] Evidence also demonstrates a tendency for anxiety disorders not to be adequately diagnosed or addressed in SMI patients.[3, 5]

People with SMI have a higher prevalence of Type II Diabetes (DM2) than age/sex matched controls without SMI [8-10], and also have more overall medical illness burden.[11-17] Some of that pathology can be attributed to the use of psychotropic medication such as second generation antipsychotics.[18-21] However, the phenomenon of impaired glucose

tolerance in SMI patients was well documented before the introduction of either first-or-second generation antipsychotics.[22, 23]

There also exists a complex set of interrelated factors that lead patients with SMI to get less-than-adequate care for their medical comorbidities (stigmatization within healthcare systems, access challenges related to financial and cognitive difficulties, patient behavior, and systems-based challenges relating to coordination of care, etc).[24] [12, 25] Evidence also points toward hyperactivity of the HPA Axis in patients living in conditions of chronic stress and anxiety, along with an associated tendency toward inflammatory immune states that can lead to impaired glucose metabolism.[26-28] Thus, SMI patients with DM2 face a constellation of vulnerabilities, the interactions and effects of which are not well understood.

The Targeted Training in Illness Management (TTIM) study for individuals with Serious Mental Illness and Diabetes Mellitus Study is an ongoing project testing a novel self-management vs. treatment as usual . TTIM is designed to be practical in a primary care system and to improve mental health and general health outcomes.[29-31] Little data currently exist regarding the interplay between comorbid anxiety, clinical course of DM2, and overall medical burden in the SMI population. This analysis aimed to identify the rates of comorbid anxiety in people with SMI and DM2 and assess DM2 management in those with comorbid anxiety as measured by hemoglobin A1c (HbA1c) levels compared to SMI patients with DM2 who do not have anxiety . We also set out to study associations with overall medical burden in those with and without anxiety as measured by Charlson scores.

Methods

This analysis was derived using baseline data from the first 157 participants enrolled in a large NIMH-funded study designed to test a novel intervention (TTIM) vs. treatment as usual (TAU) among individuals with SMI and comorbid diabetes (1R01MH085665, PIs: Sajatovic & Dawson). The study is a randomized controlled trial (RCT) involving 200 individuals with SMI and is being conducted in a safety-net health system primary care setting. Primary measures include SMI symptoms (Montgomery Asberg Depression Rating Scale; MADRS; Brief Psychiatry Rating Scale: BPRS) and diabetes control (HbA1c levels). Secondary outcomes include disability, alcohol use, diabetes knowledge, social support, insight, treatment adherence, and body weight.

Participants

Inclusion criteria included (1) a diagnosis of and current treatment for schizophrenia, schizoaffective disorder, bipolar disorder or depression as confirmed by the Mini-International Neuropsychiatric Interview (MINI--Sheehan [32]); (2) DM2 diagnosis based upon previous records or laboratory values; (3) at least 18 years of age; (4) able to communicate in English; and (5) able to provide written, informed consent to participation. Individuals under guardianship required written consent from both the subject and guardian. Exclusion criteria included (1) actively suicidal/homicidal; (2) unable to be rated on study rating scales; (3) a diagnosis of dementia; (4) pregnancy; (5) psychiatric symptoms severe enough to preclude participation in groups; (6) unable to provide informed consent; or (7) physical and/or dietary needs that would preclude the TTIM Intervention. The study was

approved by the local institutional review board (IRB). Study participants were recruited from clinician and community referrals, word of mouth and self-reported referrals in response to IRB-approved advertisement, and via electronic health record search for having SMI on the medical problem list.

Measures

In addition to demographic and clinical variables presence and type of comorbid anxiety was measured with the Mini International Neuropsychiatric Inventory (MINI).[32] Diabetes control was evaluated using baseline HbA1c levels, which provide an indication of relative blood glucose control over the previous 3 months. A self-reported Charlson Index evaluated the presence of significant medical comorbidity [33].

Data Analysis

Analyses were conducted in SAS Version 9.2 and R program. We report descriptive statistics, including means and standard deviation within SMI diagnosis groups of individuals with schizophrenia/schizoaffective disorder, bipolar disorder or major depression in Table 2. We also report the p-value from the nonparametric Kruskal–Wallis one-way analysis of variance by ranks across diagnostic groups. Bivariate Spearman correlations between HbA1c and anxiety load (measured by answers to selected MINI items), both overall and within the three SMI diagnosis groups were assessed. The same analysis was conducted between Charleson score and anxiety load. A series of linear regression models that controlled for severity of depression were used to examine if the correlation between the dependent variable HbA1c and the independent variables (anxiety load and SMI diagnosis group) changed after controlling for covariates of interest. We then performed residual analysis and made appropriate transformations to the data when necessary, if regression assumptions were violated. As a result of the residual analysis, we use the logarithm transformation for HbA1c. We defined $\alpha = 0.05$ for our level of significance in all statistical tests, and all statistical tests are two-tailed.

For purposes of this study, all DSM-IV anxiety disorder diagnoses were included except for Obsessive Compulsive Disorder, based on agreement by study investigators that OCD patients were not representative of the anxiety cohort as a whole.

Results

Sample Description

In this baseline sample of 157 patients, roughly half (N=77) carried a diagnosis of major depression, with the remainder divided evenly between schizophrenia/schizoaffective disorder (N=40) and bipolar disorder (N= 40). Fifty-two (33.1%) had at least one comorbid anxiety diagnosis. The mean age for the sample was 52.9 (SD 9.8), which contained more women than men (N=102 vs. N=55, respectively). 40% were African American (N=62), 9% were Hispanic (N=14) and 10% classified themselves as “Other”. (N=15). The average subject had 12.6 years (SD 2.6) of education and had carried SMI and DM2 diagnoses for 18.1 and 10.4 years, respectively. Psychiatric symptom severity averaged in the moderately to severely depressed range (MADRS total score), while psychotic symptom range was of

relatively low severity (BPRS). Table 1 illustrates proportion of individuals with specific types of anxiety disorder and a relative comparison to reported U.S. samples with schizophrenia, DM2 and the general U.S. population.

Demographic and Clinical Differences between Anxiety/Non-Anxiety Sub-groups

Individuals with SMI, DM2 and at least one anxiety disorder were younger and had higher depression, psychotic and global symptom severity, greater disability, more stigma and discrimination experience, more social withdrawal, and less social support. We did not find a significant association between having at least one anxiety diagnosis and poorer glucose control. “Total anxiety load”, as measured by cumulative number of anxiety diagnoses, was also not significantly associated with HbA1c score. Of the clinical factors we examined, only depressive symptoms were found to be significantly associated with poorer diabetes control.

Discussion

Anxiety disorders are found in 1 in 3 people who have both an SMI and DM2 diagnosis. To the best of our knowledge, this is a novel finding that lines up well with previously published work regarding elevated anxiety rates among individuals with either SMI or anxiety alone. One study (N=100) found that across subpopulations of individuals diagnosed with bipolar disorder, schizoaffective disorder, or schizophrenia, rates of comorbid anxiety were consistently in the 43-45% range.[5] A study of individuals with schizophrenia found that 15% met criteria for panic disorder and 29% met criteria for PTSD[4], while another with a similar population (N=53) found that individuals with comorbid anxiety had more difficulties globally, at work, and in social settings than peers without such comorbidities.[2] Literature supports a multifactorial etiology for such elevation, including fear and uncertainty related to social rejection, diminished socioeconomic status, and homelessness. [3, 5, 34-37]

Elevated rates of anxiety in DM2 patients have been well-demonstrated by previous studies and are linked to combined effects of functional disability, pain, and uncertainty inherent to life with a chronic illness such as DM2, especially as the disorder progresses to include complications such as peripheral neuropathy, vision loss, and limb amputation.[38-41]. Interestingly, several risk factors for increased anxiety in DM2 individuals that were cited by one of these studies—smoking, history of alcohol abuse, poor glycemic control, and complications of DM2—are known to have an elevated prevalence in individuals with SMI. [39, 42, 43] In individuals with an SMI diagnosis, DM2 onset and intensity have been linked to SMI-influenced factors such as diet, medication side effects, and the effect of cognitive impairment on ability to proactively manage a chronic and complex disease.[18, 19, 22, 34, 44, 45]

The finding that anxiety was associated with increased rates of depression and decreased function in the TTIM population is not at all surprising, given evidence that long-term anxiety can trigger and exacerbate core symptoms of depression such as sleep, mood, energy, concentration, appetite, and feelings of hopelessness, thus negatively impacting function.[46-49] .In contrast to our original hypothesis we did not find that comorbid anxiety

in people with comorbid SMI and DM2 had worse DM2 control. Reasons for this cannot be ascertained from our cross-sectional methods that do not allow for interpretation of causality. Perhaps anxiety makes individuals more aware of the risks involved in poorly managed DM2 and they are more conscious of the need to control their diet and weight. Among other studies we examined relating the effect of both anxiety and depression to DM2-related parameters such as HbA1c, all showed depression to be significantly related while only a few found this association for anxiety.[25, 48, 50-52] This also held true when looking at broader outcomes such as overall mortality.[53] Perhaps depressive symptoms are a “downstream” effect in terms of illness chronology and anxiety could be a precursor to overall worsening SMI that only become evident over time. The literature suggests that clinicians may be less aggressive in treatment of schizophrenia in individuals with comorbid diabetes.[54] Longitudinal studies are needed to evaluate these causal relationships.

Limitations

Limitations associated with this study included sample size, inability to determine causality from a cross-sectional baseline sample, and the possibility that the sample studied is not representative of the broader population of patients with SMI and comorbid diabetes. Factors such as cognitive deficits and paranoia could ostensibly impact diabetes control and may act independently of symptom severity, e.g. ability to follow instructions relating to a treatment plan and willingness to do so if suspicious of care providers. Strengths of the analysis include a well characterized population whose SMI diagnoses were confirmed by DSM criteria as well as recruitment from a safety-net primary care setting that treats medically complex individuals with SMI.

Conclusions

Individuals living with both SMI and DM2 are vulnerable to anxiety, depression, and decreased function. The effects of depressive symptoms, in particular, put them at risk for poor glucose control and thus increased complications of DM2 and decreased quality of life. Further study is necessary to determine what changes may be needed in systems that care for these patients in order to prevent outcomes that are painful, disabling, costly, and life-threatening. Data currently available, such as that provided by this baseline study, is not sufficient to determine when and how best to intervene, thus suggesting the need for larger, longitudinal studies.

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Table 1

Comorbid anxiety among TTIM subjects compared to national averages

Anxiety Disorder	TTIM Subjects N=157	US Mean for Patients with Schizophrenia [3] (95% CI)	US Mean, DM2 Patients [38] (no CI available)	US Mean, General Population[1] (%, se)
Panic disorder	24(15.3%)	9.8% (4.3%-15.4%)	1.3%	2.7% (0.2)
Agoraphobia	24(15.3%)	5.4% (0.2%-10.6%)	4.6%	0.8% (0.1)
Social phobia	27(17.2)	14.9% (8.1%-21.8%)	7.3%	8.7% (0.4)
PTSD	21(13.4)	12.4% (4.0%-20.8%)	1.2%	3.5% (0.2)
GAD	34(21.7%)	10.9% (2.9%-18.8%)	13.5%	3.1% (0.3)
One or more anxiety disorders	52(33.1%)	38.3% (26.3%-50.4%)	14%	18.4% (0.7)

Table 2

Characteristics of SMI patients with and without a comorbid anxiety diagnosis

	Anxiety (N)	Mean (STD)	No Anxiety (N)	Mean (STD)	P value
Age	52	51.28(10.15)	105	54.19(9.50)	0.0430
Yrs education	49	12.49(2.80)	95	12.63(2.56)	0.2254
Yrs w/ SMI diagnosis	52	17.88(11.92)	104	18.18(12.58)	0.9955
Yrs w/ DM2 diagnosis	50	10.21(9.45)	104	10.43(7.31)	0.2870
GAF	52	51.40(11.42)	105	52.35(11.56)	0.5191
MADRS	51	27.37(10.04)	105	22.23(8.49)	0.0006
BPRS	51	41.94(11.45)	105	38.20(8.32)	0.0493
SF36v1	52	3.96(0.86)	105	3.74(0.95)	0.1898
CGH	52	4.48(0.92)	105	4.15(0.93)	0.0225
Sheehan Disability	52	19.12(6.35)	105	16.42(6.15)	0.0047
AUDIT	52	0.90(2.16)	100	2.09(5.21)	0.3272
CAGE	51	1.12(1.66)	105	0.62(1.28)	0.0617
DAST	51	0.86(2.25)	102	0.46(1.60)	0.0571
Diabetes Knowledge	51	67.28(20.18)	105	66.47(19.99)	0.7639
MSPSS	50	39.50(9.68)	96	43.00(9.82)	0.0158
Glucose Control Total	21	2.22(0.97)	51	1.64(0.49)	0.0123
	41	2.76(1.29)	88	2.49(1.39)	0.1696
	28	2.30(0.96)	68	1.71(0.71)	0.0006
	39	2.02(1.28)	85	1.60(0.94)	0.0790
Glucose Medication	40	1.76(1.16)	80	1.37(0.79)	0.2349
PDSMS	51	24.90(6.55)	101	26.47(6.63)	0.1411
PMHSMS	48	23.98(6.40)	101	27.85(6.07)	0.0007
ITAQ	48	19.75(3.44)	83	16.69(5.77)	0.0038
ISMI Alienation Stereotype endorsement Discrimination exp Social withdrawal Stigma resistance	50	19.56(5.51)	101	15.85(5.82)	0.0006
	49	15.47(4.44)	98	13.31(4.45)	0.0070
	50	15.80(4.71)	99	10.94(4.38)	<0001
	50	17.84(5.78)	101	13.34(5.01)	<0001
	50	7.52(2.67)	104	6.17(3.38)	0.0010
BMI	49	37.00(10.04)	98	35.80(8.54)	0.6190

	Anxiety (N)	Mean (STD)	No Anxiety (N)	Mean (STD)	p value
Hb1ac	52	7.92(2.18)	104	8.11(2.51)	0.8568
Charlson	52	2.06(1.76)	105	2.14(1.45)	0.6030
TRQ (week)	57	12.11	88	21.66	0.47
TRQ(month)	57	3.57	88	5.60	0.31

BPRS= Brief Psychiary Rating Scale, MADRS = Montgomery Asberg Depression Rating Scale, CGI = Clinical Global Impressions, GAF= Global Assessment of Functioning, MSPSS=Multidimensional Scale of Perceived Social Support, ITAQ=Insight and Treatment Attitudes Questionnaire, TRQ= Tablets Routine Questionnaire, CAGE= standardized measure to assess problem drinking, DAST-10=Drug Abuse Screening Test 10-item version; SF36v1=MOS 36-Item Short-Form Health Survey; AUDIT=Alcohol Use Disorders Identification Test; PDSMS=Perceived Diabetes Self-Management Scale; PMHSMS=Perceived Mental Health Self-Management Scale; ISMIS=Internalized Stigma of Mental Illness Scale; BMI=Body Mass Index; Charlson=Charlson Comorbidity Index; TRQ=Tablet Routines Questionnaire