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Is It Anxiety, Depression, Or Bipolar Disorder? – Patient at Doctors' Mercy or Doctor at Patients' Mercy?

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Abstract*: Is it anxiety, depression, or bipolar disorder? This is the question not easily answered even by an expert on the subject .Not only do their diagnostic features overlap, but also anxiety disorders (Panic Disorder, Obsessive Compulsive Disorder, Social Anxiety Disorder, Phobias), may be comorbid with any of the rest of the two, as can depression (mild, moderate, severe) be co-morbid with anxiety disorders, like say Obsessive Compulsive Disorder. The similarities and differences between these two conditions, as well as many of the important features of the comorbidity of these disorders, are well understood. Given the substantial overlap between symptoms of BPD and other psychiatric conditions, an accurate cross-sectional assessment is inherently difficult to achieve. Over the course of my own psychiatric practice, this has invariably been the finding, as has been described in this article. Anxiety symptoms and syndromes are highly prevalent among patients diagnosed with Bipolar Disorders, affecting approximately half of types I and II Bipolar Disorder patients at some time. Accordingly, anxiety symptoms and syndromes require thoughtful consideration in the comprehensive assessment and treatment of these patients over time. In addition, mood disorders should be considered in assessing patients considered to have a primary anxiety disorder. In addition to the above difficulty, other factors like overcrowded OPDs, counter-transference on the part of the psychiatrist, avoidance, hostility on the part of the patient, are other contributing factors that can lead to missing of the correct diagnosis or its associated comorbidities. Why and how this occurs needs to be found out , not just for not labeling a wrong diagnosis on the patient, but also for a much better understanding of the disorder, that the patient is suffering from and its pathogenesis. Making the proper diagnosis, thus, not only requires knowledge of these subtle factors, but also the input, in terms of time and patience of both the psychiatrist as well as the patient.*

Key Words*: anxiety, depression, bipolar disorder, co-morbidity.*

I. Introduction

Anxiety, Depression and Bipolar disorders are among the most common illnesses in the community. Patients with depression often have features of anxiety disorders, and those with anxiety disorders commonly also have depression. Both disorders may occur together, meeting criteria for both. Bipolar Affective Disorder, too, can have features of Anxiety Disorder (Panic Disorder most commonly). It can be difficult to discriminate between them but it is important to identify and treat both illnesses, as they are associated with significant morbidity and mortality.

Bipolar disorder (BPD) is highly prevalent and heterogeneous. Its increasing complexity is often caused by the presence of comorbid conditions, which have become the rule rather than the exception. Lifetime prevalence of psychiatric co-morbidity has been reported in community and clinical studies. Most (95%) of the respondents with BPD in the National Co-morbidity Survey met criteria for three or more lifetime psychiatric disorders.[1] In a Stanley Foundation Bipolar Treatment Outcome Network study of almost 300 patients, 65% met *DSM-IV* criteria for at least 1 co-morbid Axis 1 disorder.[2]Anxiety may be interwoven into the fabric of syndromic bipolarity, may occur alongside it as a comorbid condition, and may occur in sub-syndromal bipolar states as well.[3]Patients with BPD are at higher risk for many other anxiety subtypes, including generalized anxiety disorder, simple phobia, social phobia, obsessive-compulsive disorder, posttraumatic stress disorder, and panic disorder.[1,2] Of these, panic disorder appears to have the highest risk of co-morbidity. In general, anxiety tends to predict an earlier age at onset of BPD and results in a more complicated and severe disease course.

The central tenet of clinical co-morbidity, the occurrence of two syndromes in the same patient, presupposes that they are distinct categorical entities. By this definition, two or more coexisting syndromes do not negate one another, nor paradoxically does this coexistence negate the potential for one to influence the course, outcome, and treatment response of the other. Isolating a syndrome by characterizing it through a unique pathogenic process allows for diagnostic fidelity even while acknowledging overlapping phenotypes.[3]

Developmentally, anxiety disorders are almost always the primary condition, with onset usually occurring in childhood or adolescence.[4] co-morbidity of anxiety and depression is explained mostly by a shared genetic vulnerability to both disorders, or by one disorder being an epiphenomenon of the other.[5]

II. Observations

For proper management of psychiatric patients, the most important step is the making of a proper diagnosis for the patient, including the comorbidities as well. This, however to be exact, needs not only complete process of history taking in detail along with detailed past psychiatric history but interviewing the patients informant in detail, as well. Corroborating history from informants, who are reliable enough and staying with patient for an appropriate period, so as to be able to supply the necessary information, is instrumental in this process. No doubt all this needs sufficient time input by the doctor, patient, as well as the informants. Fallacies in any of the above steps, invariably leads to misdiagnosis and hence mismanagement for the patient. If carefully made, the diagnosis stands the test of achieving remission for the patient, giving the psychiatrist a pat on the back, but as we all know, this is not always the case. Most patients with an adequate history and mental status examination are properly diagnosed as well as managed and feel well satisfied with the doctors' efforts. Few, however, remain a mystery, where adequate and reliable history is not available, or no informant is available and the psychiatrist is on his own discretion. Overcrowded OPDs, countertransference on the part of the psychiatrist, avoidance, hostility on the part of the patient, are other contributing factors leading to missing of the correct diagnosis or its associated comorbidities.

Notwithstanding all these above factors, the diagnostic entities of depressive disorder, anxiety disorders, bipolar disorder, may not in themselves allow explanation of all the symptoms of the patient, nor do the symptoms justify a separate Axis 1 diagnosis to be made. This can only be due to presence of some features of a particular disorder, not all as required in a diagnosis. Missing on these naturally alters the treatment protocol.

Subsyndromal symptoms were assessed in longitudinal, prospective follow-up of a cohort of patients with bipolar disorder by MacQueen GM et al, in 2003.[6] Findings of study show that Bipolar disorder (BD) is associated with measurable levels of functional impairment that persist beyond the period of acute, syndromal illness.

But, the factors contributing to this impairment are not well described. Patients with sub-syndromal symptoms had high rates of co-morbid anxiety disorders, and were more likely to have increased rates of eating disorder as well. Patients with sub-syndromal symptoms had lower global assessment of functioning (GAF) scores than euthymic patients, and had as many clinic contacts and medication trials as patients with full episodes of illness. A key variable influencing inter-episode function may be residual mood symptoms. The contribution of persistent subsyndromal symptoms to disability in unipolar major depression has been known. Factors such as neuropsychological impairment, now well described in euthymic bipolar patients, may contribute to interepisode impairment in a portion of patients.

III. Discussion

Co-morbid anxiety symptoms and disorders must be considered when diagnosing and treating patients with bipolar disorder. Conversely, patients presenting with anxiety disorders must be assessed for co-morbid mood disorders, including bipolar disorder. Patho-physiological, theoretical, and clinical implications of the overlap of bipolar and anxiety disorders are discussed.

How might the extensive overlap of bipolar disorder with these other axis I disorders be explained? One possibility is that these disorders are in fact distinct but unrelated disease entities, representing either risk factors for each other or the sharing of similar end states from different etiologic mechanisms. This possibility is supported in part by the findings of high rates of substance use disorders in the families of patients with comorbid substance use disorder, suggesting the inheritance of two (or more) illnesses in some patients. Another possibility, however, is that bipolar disorder is related to substance use, anxiety, and eating disorders (or at least some forms of these disorders) and, by extension, that all of these disorders may be related to one another and share a common underlying patho-physiologic etiology.

The relationship of panic disorder to other anxious-phobic and depressive state has been known for some time. Data by Giulio Perugi et al,[7] extends this relationship to soft bipolar disorders. In discussing anxious–bipolar comorbidity, this study by Perugi et al, focuses on panic-agoraphobic (PD), social phobic (SP), and obsessive-compulsive disorders (OCD). Excluded from this discussion is generalized anxiety disorder, for which there exists increasing evidence of a shared common diathesis with unipolar major depression. Frequent comorbidity among PD, SP, OCD, and mood disorders has been widely reported in clinical and epidemiologic studies. Much of this research, however, has been essentially limited to the co-occurrence of anxiety disorders and unipolar depression. This narrow viewpoint is being increasingly challenged, and the available evidence strongly suggests that comorbidity between anxiety and mood disorders—conventionally conceived as the relationship between anxiety and depression—extends into the domain of bipolar spectrum disorders.

Study in 2002, by Freeman M P et al [8,] in which he reviewed a growing number of epidemiological studies and found that bipolar disorder significantly co-occurs with anxiety disorders at rates that are higher than those in the general population. Clinical studies have also demonstrated high comorbidity between bipolar

disorder and panic disorder, OCD, social phobia, and post-traumatic stress disorder. Psychobiological mechanisms that may account for these high comorbidity rates likely involve a complicated interplay among various neurotransmitter systems, particularly norepinephrine, dopamine, gamma-aminobutyric acid (GABA), and serotonin. The second-messenger system constituent, inositol may also be involved. Little controlled data are available regarding the treatment of bipolar disorder complicated by an anxiety disorder.

Anxiety and its correlates were examined by Simon NM et al [9], in 2004, in a cross-sectional sample from the first 500 patients with bipolar I or bipolar II disorder enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder, a multicenter project funded by the National Institute of Mental Health designed to evaluate the longitudinal outcome of patients with bipolar disorder. Lifetime comorbid anxiety disorders were common, occurring in over one-half of the sample, and were associated with younger age at onset, decreased likelihood of recovery, poorer role functioning and quality of life, less time euthymic, and greater likelihood of suicide attempts. Although substance abuse disorders were particularly prevalent among patients with anxiety disorders, comorbid anxiety appeared to exert an independent, deleterious effect on functioning, including history of suicide attempts (odds ratio=2.45, 95% CI=1.4-4.2). Thus, an independent association of comorbid anxiety with greater severity and impairment in bipolar disorder patients was demonstrated, highlighting the need for greater clinical attention to anxiety in this population, particularly for enhanced clinical monitoring of suicidality. In addition, it is important to determine whether effective treatment of anxiety symptoms can lessen bipolar disorder severity, improve response to treatment of manic or depressive symptoms, or reduce suicidality.

The below mentioned study by Lisa D Hawke et al[10], in 2013, examines the impact of comorbid anxiety disorders on response to two psychosocial interventions for Bipolar Disorder. A sample of 204 patients with BD took part in the study. Of them, 41.7% had a comorbid anxiety disorder. All participants received either individual cognitive behavioral therapy or group psycho education for BD. Evaluations included complete pretreatment and 18-month follow-up assessments of mood and anxiety symptoms, functioning, medication compliance, dysfunctional attitudes, and coping style. Outcome was compared based on the presence or absence of a comorbid anxiety disorder. The participants with comorbid anxiety disorders ranked more severe than those without on several measures. Despite more severe illness characteristics, the magnitude of their treatment gains was equivalent or superior to that of the participants without anxiety disorders on a variety of outcome measures. Although the treatments did not specifically target the anxiety disorder, the participants made significant improvements in anxiety symptoms. Despite greater illness severity, patients with comorbid anxiety disorders can make substantial gains from psychosocial interventions targeting BD. Even in the presence of an anxiety disorder, they are able to attend to the content of the psychosocial treatments and apply it to better manage their condition. The presence of a comorbid anxiety disorder should not be considered a deterrent to offering BD-focused psychosocial treatments.

Anxiety and depression, when combined are more severe, have a greater risk of suicide and are more disabling and more resistant to treatment. They result in more psychological, physical, social and workplace impairment than either disorder alone outcomes.

John WG Tiller, in 2013, [11,] studied the impact of comorbid depression and anxiety on patients, how it can increase impairment and health care use, compared with either disorder alone. Comorbid depression and anxiety are common and affect up to a quarter of patients attending general practice. Screening for comorbidity is important, as such patients are at greater risk of substance misuse, have a worse response to treatment, are more likely to remain disabled, endure a greater burden of disease, and are more likely to use health services in general. There are effective treatments for specific disorders, but a paucity of data about treatment for anxiety and depression comorbidity. More than a third of patients with a mental disorder do not seek treatment, and almost half are offered treatments that may not be beneficial. This suggests the need for further public awareness and professional education that can enhance clinical practice, promoting better mental health.

The co-occurrence of anxiety and bipolar disorders was studied in detail by Gustavo H Vazquez et al [12] in 2014, in which they reviewed epidemiologic, clinical, and treatment studies of the co-occurrence of BD and anxiety disorder through electronic searching of Pub med/MEDLINE and EMBASE databases. The results showed that nearly half of BD patients meet diagnostic criteria for an anxiety disorder at some time, and anxiety is associated with poor treatment responses, substance abuse, and disability. Reported rates of specific anxiety disorders with BD rank: panic ≥ phobias ≥ generalized anxiety≥ posttraumatic stress ≥ obsessive-compulsive disorders. Their prevalence appears to be greater among women than men, but similar in types I and II BD. Anxiety may be more likely in depressive phases of BD, but relationships of anxiety phenomena to particular phases of BD, and their temporal distributions require clarification. Adequate treatment trials for anxiety syndromes in BD patients remain rare, and the impact on anxiety of treatments aimed at mood stabilization is not clear.

IV. Conclusion

There has been growing interest and concern about the high rates of comorbidity of anxiety disorders and depression, now clearly documented in both epidemiologic and clinical samples. The presence of comorbidity has been repeatedly shown to have a negative impact on course, including elevated rates of suicidality, greater severity of the primary disorder, greater impairments in social and occupational functioning, and poorer response to treatment.

A careful longitudinal assessment that establishes a chronology of onset of different conditions, a symptom and functional profile between mood episodes, the course of illness, and response to treatment are essential for a more robust diagnosis.[13,14] Furthermore, the inherent challenge in obtaining an accurate history from a bipolar patient—especially one with comorbidities—requires corroboration from family members.

V. Limitations

Although clinical guidelines for BPD acknowledge the complexity of treating the illness, most have limited recommendations specific to the patient with co-morbidities. This may reflect the limited nature of the clinical evidence in this field.[14] the cost of diagnostic and therapeutic uncertainty, however, is calculated through the high cost of chronicity, with elevated rates of suicide, legal and interpersonal difficulties, and repeated hospitalizations Missing patients diagnosis often occurs in setups where OPDs are crowded, as is often the case in our country. Co-morbidities are at times missed and if diagnosed, not adequately managed. Anxiety symptoms of bipolar patients tend to be under recognized.

VI. Recommendations

This study, underlines the importance of this topic, not only as it assists in diagnosing the patients correctly, but also in managing them appropriately. Anxiety disorders (panic disorder, which is found to be the most prevalent), if detected earlier in the course of bipolar disorder , predicts a much better treatment outcome in the patient, while missing it altogether, may result in patient dropout. Further, we realized that missing those subtle hypomanic symptoms may result in converting a plain depressive or anxiety disorder patient to full blown mania. Researches also document which anti-anxiety medications are less likely to shift a patient to mania and which are considered safer. Ongoing studies in this direction are needed for better patient care Further researches in this field are needed for the better management of the patient. Debate is truly called for whether Diagnostic guidelines (DSM or ICD), should also make some changes to make it easier to diagnose patients more accurately. The identification of differential patterns of co-morbidity may provide important information in distinguishing more homogeneous clinical subtypes of affective disorders from the genetic, temperamental, and therapeutic point of view.

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