The Impact of Substance Abuse on the Severity of Manic Relapse in Bipolar Patients

Thesis

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SUMMARY

BAD In the World Health Organization Global Burden of Disease Study ranked sixth among all medical disorders in terms of years of life lost to death or disability **(Godwin, 2003)**. It is a severe and often chronic disorder with lifetime prevalence rates up to 6.5% in the general population **(Vornik and Brown, 2006)**. Studies have demonstrated that the annual costs of BAD to the society range from 1.8 to 45 billion US dollars; indirect costs due to work absence are the most important ones **(Hakkaart et al., 2004).**

BAD is defined by discrete episodes of mania and, almost invariably, depression; of course, patients can present in either of the two poles of illness **(Kaplan and Sadock, 2009)**.

Rates of psychiatric co morbidity with BAD were high, with anxiety disorders, problematic substance use, and suicidality **(Nicole Kozloff et al., 2010)**.

High rates of SUD have also been documented in both inpatient and outpatient populations of individuals with BAD. More than14 studies conducted with bipolar patients in both inpatient and outpatient psychiatric settings, reported that the lifetime rates of drug abuse or dependence for patients with bipolar disorder ranged from 14%–65% compared with rates of 6%–12% in the general population **(Brown et al., 2001)**.

First thanks to **ALLAH** *to whom I relate any success in achieving any work in my life.*

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This work is dedicated to …

My beloved father, to whom I owe everything I ever did in my life and will achieve.

My mother for always being there for me

My brothers and my sister for their support

Finally my husband and my lovely son for being the light of my life

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List of Abbreviations

5HT	*5 Hydroxy Tryptamine.*
AIAQ	*Anger, Irritability and Assault questionnaire.*
ASI	*Addiction Severity Index.*
ASPD	*Anti Social Personality Disorder.*
AUD	*Alcohol Use Disorder.*
BAD	*Bipolar Affective Disorder.*
DAT	*Dopamine Transporter.*
DD	*Dually Diagnosed.*
DLPFC	*Dorso Lateral Pre Frontal Cortex.*
ECA	*Epidemiolgical Catchment Area.*
GABA	*Gamma Amino Butyric Acid.*
Gln	*Glutamine.*
Glu	*Glutamate.*
GRK-3	*G-Protein Receptor Kinase-3.*
G1,2	*Group1,Group2*
IL I, II	*Interleukin I,II*
MDD	*Major Depressive Disorder.*
MRI	*Magnetic Resonance Imaging.*
MRS	*Magnetic Resonance Spectroscopy.*

NAA	*N Acetyl Aspartate.*
NMDA	*N- Methyl D- Aspartate.*
PCr	*Phospho Creatine.*
PSUD	*Poly Substance Use Disorder.*
PTSD	*Post Traumatic Stress Disorder.*
QOL	*Quality of Life.*
SCID-I	*Structured Clinical Interview for DSM-IV-I.*
STEP-BD	*Systematic Treatment Enhancement Program for Bipolar Disorder.*
SUD	*Substance Use Disorder.*
YMRS	*Young Mania Rating Scale.*

INTRODUCTION

Bipolar Affective Disorder (BAD) — is not simply disorder of excessive happiness, as the core symptoms of mania or hypomania include poor concentration, agitation, and impaired judgment. These symptoms commonly lead to impairment in important social roles and help seeking in general medical settings. So the effects of this disorder extend beyond internal distress to a range of effects on family members, employers, health care systems, and taxpayers **(Gregory and Simon, 2003).**

In the World Health Organization Global Burden of Disease Study, BAD ranked the sixth among all medical disorders in terms of years of life lost to death or disability **(Godwin, 2003)**. It is a severe and often chronic disorder with lifetime prevalence rates up to 6.5% in the general population **(Vornik and Brown, 2006)**. Studies have demonstrated that the annual costs of BAD to the society range from 1.8 to 45 billion US dollars; indirect costs due to work absence are the most important ones ***(Hakkaart et al., 2004).***

The natural course of BAD is characterized by a constant risk of recurrences over a patient's life span, even 30 to 40 years after onset and up to 70 years of age or more, causing impairment of psychosocial functioning, despite the advances in pharmacological and non-pharmacological treatments **(Tohen et al., 2009)**. The influence of modern treatment

interventions on the natural course of illness is uncertain. While considered to have a more favorable prognosis than schizophrenia, it is not uncommon for BAD to include persisting alterations of psychosocial functioning. Although long-term symptomatic remission does not guarantee functional recovery, it may have a favorable impact on overall prognosis **(Angst et al., 2003).**

Although the functional impairment of bipolar patients is usually attributed to depressive and manic episodes, high rates of unemployment have been described even in clinically remitted patients **(Zarate et al., 2000).**

It seems that quality of life, as determined by illness intrusiveness, is compromised in subjects with BAD even during periods of euthymia. BAD is at least as intrusive as several other chronic medical conditions **(Robb et al., 1998)**.

BAD presents many challenges to an individual's social network **(Perlick et al., 2007)**. BAD in older adults may have an especially strong impact on family and friends because of the physical and cognitive impairments that often co-exist with mood disorders in late life **(Gildengers et al., 2007).**

BAD has a typical onset in adolescence or young adulthood, an age normally associated with increasing independence and the establishment of future professions and significant relationships **(Grant et al., 2005)**. When BAD presents during this critical period, it can have a profound

impact, and is clinically associated with poor prognosis in young adulthood and beyond **(Leverich et al., 2007)** even when they receive mental health services, young patients with BAD are often misdiagnosed with other conditions such as unipolar depression **(Perlis et al., 2005)**.

Observational long-term studies on patients with BAD reported persistent impairment with significant disability, including 19% to 23% of months with moderate impairment and 7% to 9% of months with severe overall impairment **(Tohen et al., 2003)**.

In a study by **Judd et al. (2008**) he found that Patients with BAD I were unable to carry out work role functions during 30% of assessed months, which is significantly more in comparison to patients with unipolar major depression or BAD II (21% and 20%, respectively). This degree of disability is similar to that of schizoaffective disorders.

Despite the recent increase in the diagnosis and treatment of BAD in the younger population (**Moreno et al., 2007)**, only a minority access treatment **(Leverich et al., 2007)**.The under-recognition and misdiagnosis of BAD are major barriers to effective treatment **(Perlis, 2005)**.

Substance use disorder (SUD) is common in BAD, even from the first episode **(Baethge et al., 2005)**. In results from the Epidemiologic Catchment Area Study(ECA), bipolar I patients had a substance use prevalence rate of 60.7% and bipolar II

patients had a substance use prevalence rate of 48.1% **(Regier et al., 1990)**. The life time rates of drug use or dependence for patients with BAD ranged from 14%–65% compared with rates of 6%–12% in the general population **(Brown et al., 2001)**. Alcohol and cannabis are the substances most often used, followed by cocaine and then opioids **(Cerullo and Strakowski, 2007)**.

Data from studies of BAD adults also suggest that the risk for SUD is particularly high in those adults who had the onset of their BAD prior to age 18 years**.** For instance**, Lin et al. (2006)** showed that earlier onset BAD was associated with a higher risk for SUD in adults than later onset (e.g. adult onset) BAD.

A limited literature exists suggesting that juvenile onset BAD may be a major risk factor for SUD. For instance, an excess of SUD has been reported in adolescents with BAD **(Birmaher and Axelson, 2006)** and BAD appears over-represented in youth with SUD **(Deas and Brown, 2006)**.

SUD may be a symptom or precipitant of BAD, BAD and SUD may share common risk factors such as impulsivity **(Swann et al., 2005)**, co morbidity with anxiety disorder **(Goldstein and Levitt, 2008)** or sensation seeking **(Bizzarri et al., 2007b)**. SUD can be a coping mechanism for managing the early symptoms or prodromes of manic and depressive episodes before the full episode of mania or depression appears **(Lam and Wong, 2005).**

Negative outcomes have been reported in patients with BAD and co morbid SUD including suicide **(Isometsa, 2005)**, suicide attempts **(Simon et al., 2007)**, poor insight and denial of illness **(Salloum and Thase, 2000)**, also A highly prevalent subgroup of BP patients with an elevated probability of poor medication adherence is represented by individuals with a co-occurring SUD **(Manwani et al., 2007)**.

SUD co-morbidity might be a factor which significantly contributes to poor social adjustment and more severe recent course of the disorder in patients with BAD, approaching the severity observed in patients with schizophrenia with no associated SUD **(Fabienne et al., 2010).**

Characterizing the risk and nature of the relationship between BAD and SUD in the young is of particular clinical scientific and public health importance. BAD is an increasingly recognized prevalent and persistent disorder affecting children and adolescence Thus, efforts at improving the understanding of the nature of the association between BAD and SUD in the young can lead to further refinements in efforts aimed at mitigating this risk **(Birmaher et al., 2006)**.

Therefore patients with dual diagnosis BAD and SUD form an important group of patients to study from clinical and public health perspectives ***(Bizzarri et al., 2007a)***.