

A retrospective survey analysis on Drug Abuse in Bipolar Disorder on Bangladeshi population

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*Dedicated To My Beloved Parents
& To My Research Supervisor*

Declaration by Candidate

I, Shaida Easmin Reza, hereby declare that the dissertation entitled “**A retrospective survey analysis on Drug Abuse in Bipolar Disorder on Bangladeshi population**” submitted by me to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of pharmacy, work carried out by me during the period 2017 of my research in the Department of Pharmacy, East West University,. The thesis paper has not formed the basis for the award of any other degree / diploma / fellowship or other similar title to any candidate of any University.

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Certificate by the Supervisor

This is to certify that the thesis entitled “**A retrospective survey analysis on Drug Abuse in Bipolar Disorder on Bangladeshi population**” submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of pharmacy, was carried out by Shaida Easmin Reza, ID: 2013-1-70-075, during the period 2017 of her research in the Department of Pharmacy, East West University, under the supervision and guidance of me. The thesis has not formed the basis for the award of any other degree / diploma / fellowship or other similar title to any candidate of any University.

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Certificate by the Chairperson

This is to certify that the thesis entitled “**A retrospective survey analysis on Drug Abuse in Bipolar Disorder on Bangladeshi population**” submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of pharmacy, was carried out by Shaida Easmin Reza, ID: 2013-1-70-075, during the period 2017 of her research in the Department of Pharmacy, East West University.

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Abstract

Bipolar disorder is a mental illness that the sufferer having at least one manic or approximately manic. The mood swings of the patient can last for weeks at a time or less than that. Experts believe that mainly caused by the dys-functioning of brain chemicals like noradrenalin, serotonin, and dopamine which are involved in both brain and bodily functions. These patients are prone to abuse different types of narcotics in its life. In this study our aim is to find out causative reason, abusive drugs type and influential factors that are involved in the case. To find out these we use a self made questionnaire with the help of experts and visit eight prime locations of Dhaka to find out people with abusing drugs. We surveyed over 200 people among them 30% of total population are found abusing drugs. Most of them are male (nearly 74%). Age ranges between 15-35 years are found more vulnerable, as almost 76% of total abuse occurs in this age range. The major abusive drug we found is Methamphetamine (37% cases) compared to others like Cannabis (32%) and benzodiazepine (17%). Due to drug abuse patient often suffers various symptoms like Volatile mood or mood swing (28%), sleep disturbance (17%), restlessness (14%), anxiety (10%) are some common symptoms that are recorded. Due to this problem they face poor family bonding (62%) and socially neglected.

Chapter-1

Introduction



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1.1 Bipolar Disorder

1.1.1 General Definition

Bipolar Disorder is a kind of mental disorder or illness. People having bipolar disorder go through unusual mood changes and show abnormal behavior. People having bipolar disorder feel happy or up and much more active than usual however other times feel very sad and down and much less active than usual. This is occurred for shifting his/her mental state. Having an unstable mood is one of the most clarified criteria of bipolar disordered patient. For having this unstable mental state, people with bipolar disorder face difficulties to do every day activities efficiently or to get along with friends and family members. That rises up his/her frustration level. For removing that frustration many of the bipolar disorder patient involve in taking different illicit drugs such as: Methamphetamine, Benzodiazepines, Cannabinoids. Sometimes their frustration level goes so high that they harm others or they attempt suicide. That's the most vulnerable condition of bipolar disorder.[1,2]

1.1.2 Clinical Definition

Clinically, it can be defined that, bipolar disorder is a mental illness that the sufferer having at least one manic (over excited or irritable mood) or approximately manic (hypo manic). That's why; bipolar disorder is also termed as manic depressive disorder. The mood swings of the patient can last for weeks at a time or less than that. In some cases, it can be a devastating long-lasting disorder.[3-6]

1.1.3 Types of Bipolar Disorder

Depending on the signs & symptoms of the patient bipolar disorder can be classified into **five types**. Such as follows:[2,7,8]

- I. Bipolar Disorder Type-1:** At this type of bipolar disorder, most people have both depression and mania. Mania is a condition at which the person has just a feeling of elation, high energy or being distracted. This mania caused by the influence of alcohol, drugs, or another health condition.
- II. Bipolar Disorder Type-2:** At this type of bipolar disorder, people have suffered from mild mania or hypo mania. Hypomania is just an event in which one's behavior differs from his/her normal state. And this difference is extreme enough to notice /guess about

the bipolar disorder. But hypo manic condition is less severe than manic condition. If it is influenced by any drugs or alcohol then hypo manic state isn't considered clinically.

- III. Rapid Cycling:** In this type of Bipolar disorder the person's mood can swing between highs & lows many times in one day. Women appear more likely than men to have rapid cycling. This type of Bipolar disorder increases the risk for severe depression and suicide attempts. To treat prolonged rapid cycling, antidepressants are often used.
- IV. Mixed Episode:** In this type of bipolar disorder, the person has both mania and depression simultaneously. It's marked by high energy, sleeplessness and racing thoughts. And this combined situation is raised up the suicidal tendency of the person who has that type of bipolar disorder.

1.2 Pathophysiology:

Pathophysiology is the physiology of abnormal states that causes by any particular syndrome or disease.[9,10]

The causative reasons of bipolar disorder can't be understood completely till now by the doctors. But there are some factors that influence bipolar disorder. Such as:

➤ **The Brain Chemicals:**

Experts believe bipolar disorder is partly caused by the dysfunctioning of brain chemicals which are called neurotransmitters.

There are three brain chemicals -- noradrenalin (nor epinephrine), serotonin, and dopamine which are involved in both brain and bodily functions. Noradrenalin and serotonin have been consistently linked to psychiatric mood disorders such as depression and bipolar disorder. Dopamine secretion facilitates to regulate pleasure and emotional reward through the nerve pathways within the areas of the brain. The nerve signaling & communicating system to other brain areas that is ran out by using dopamine. Disruption of it causes psychosis and schizophrenia, a severe mental disorder characterized by distortions in reality and illogical thought patterns and behaviors.

One of the brain chemicals Serotonin is connected to many functions related to our bodily mechanism such as sleep, wakefulness, eating, sexual activity, impulsivity, learning, and memory. Researchers believe that abnormal functioning of Serotonin as a chemical messenger collapse the efficiency of nervous system that is involved in accepting signals and carry them to the brain and delivering the function according to the accepted signals. For which mood disorders (depression and bipolar disorder) occurs in a person.

➤ **Genetic Factor:**

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Many studies of bipolar patients and their relatives have shown that in most cases bipolar disorder is developed in one's as an inherited disease. The most interesting studies report had obtained while studying on twins those relate the bipolar disorder with the Genetic Factor. In the studies of identical twins, scientists obtained the result of the studies that if one identical twin has bipolar disorder, the other twin has a greater chance of developing bipolar disorder than another sibling in the family. Researchers conclude a statistical findings that if one of the identical twins have bipolar disorder, the chance of developing bipolar disorder in the another twin is about 40% to 70%. [4]

The studies of Johns Hopkins University, researchers studied on all first-degree relatives of patients with bipolar I and bipolar II disorder and found that bipolar II disorder was the most common affective disorder in both family sets. In the 47 first-degree relatives of the bipolar II patients the researchers found that 40% had bipolar II disorder; and in the 219 first- degree relatives of the bipolar I patients 22% had bipolar II disorder. However, among patients with bipolar II, researchers found only one relative with bipolar I disorder. So they reported that bipolar II is the most prevalent diagnosis of relatives in both bipolar I and bipolar II families.

In other findings, researchers have reported that a person whose first-degree relatives diagnosed with bipolar I or II disorder has an increased risk for major depression in compare to the person whose first-degree relatives have no history of bipolar disorder. Scientific findings also show that the chance of affecting bipolar disorder of a person depends on the number of the affected family members and relatives by bipolar disorder. [10,11]

➤ **Environmental Factor:**

Many research shows that children of bipolar parents are often surrounded by significant environmental stressors. This indicates the environment where the children living with a parent who has a tendency toward mood swings, alcohol or substance abuse, financial and sexual indiscretions, and hospitalizations. But it is shown that every bipolar disordered parent(s) won't have children (child) with bipolar disorder, some children of bipolar parents may develop a different psychiatric disorder such as ADHD, major depression, schizophrenia, or substance abuse.

Persons who are already genetically predisposed in case of them environmental stressors play a vital role in triggering bipolar episodes. As for example a child who is growing in a family where parent (s) has bipolar disorder will suffer from lack control of moods or emotions. If the bipolar parent (s) is not medicated or if the parent is using alcohol or drugs in spite of having bipolar disorder then his/her children have to live with constant verbal or even physical abuse. [12-14]

➤ **Lifestyle:**

In most cases the life style of an individual influences a lot in developing bipolar disorder. As such:

✓ **lack of sleep :**

Loss of sleep at constantly causes the changing of mood episodes frequently thus influences the bipolar disorder. Moreover worrying about losing sleep can increase anxiety, thus worsening the

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bipolar disorder. And this deprivation of sleep leads a person to go to the manic state of bipolar disorder.

✓ **lack of physical exercise:**

Regular physical exercise helps one's to have a proper sleep. Lack of physical **exercise** increases the problem of Insomnia.

✓ **lead a stressful life:**

A stressful life gradually develops depression and this depression causes rapid changes of mood and this leads to bipolar disorder.

- ✓ **Others:** prolong sickness; phobia of something, suffering from inferiority complex, social phobia, and worst relationship with family, lack of emotional control, addiction to illicit drugs these influences the bipolar disorder.

1.3 History:

- Over **2000 years ago** at **ancient Greece** the history of bipolar disorder was first documented.

The extremes of mood '**melancholy**' (depression) and **mania** were clearly identified –as remitting fluctuating illness. The word 'melancholy' derives from '**melas**' which means **black** and '**chole**' which means **bile**. There is a reason behind this naming. The Hippocrates thought that depression resulted from an excess of **black bile**. And the word '**mania**' derives from the words 'mainesthai' and 'manis'. 'Mainestai' means 'go mad' and 'Mantis' means 'seer'. An ancient belief was that '**Mania**' is related '**menos**' which means spirit, force, passion.

The clinical term of '**melancholy**' is '**depression**' which derives from the Latin word '**Deprimere**' this means 'press down or sink down'.

- The famous Greek Physician and Philosopher **Aretaeus of Cappadocia** was the **first person** who traced the relationship between 'melancholy' and 'mania' at first century AD.

Aretaeus observed a group of patients who 'laugh, play, dance night and day, and sometimes go openly to the market crowned, as if victors in some contest of skill' but they were only to be 'torpid, dull, and sorrowful' at other times. Although he stated that both patterns of behavior resulted from one and the same disorder, this idea had brought a new direction in understanding the bipolar disorder.

- The **modern psychiatric concept** of bipolar disorder has its origins in the **nineteenth century**.

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During the 18th Century in Paris there were significant changes to how people with a mental illness were being cared for. At that time, the importance of observing and documenting illnesses was more emphasized, and the connection between **mania** and **depression** was again revived. This could be possible due to keep detailed clinical records that enabled some important re-connections to be made.

- In 1850's the **French psychiatrist** named **Jean-Pierre Falret** noted that bipolar disorder as a "**foliecirculaire**" which highlighting the circular nature of bipolar disorder, with changes from mania to depression.

"The French word "**Folie**" refers to **mania, madness, craziness** or **insanity**, with the literal translation being '**circular insanity**'. Around the same time the **French neurologist Jules Baillarger** described these extreme mood changes as the different phases of a same illness or disorder which termed as "**follié a double forme**", translated as '**dual-form insanity**'.

- However, the **German psychiatrist, Karl Kleist**, in **1953** separated out unipolar depression where there are no periods of mania or hypomania, and the term bipolar disorder was born.
- In **1899** another **German psychiatrist Emil Kraepelin** first used the term manic depressive illness to describe these phases.

Kraepelin studied the natural course of this untreated disorder and found it that this was punctuated by relatively symptom during a time interval.

On this basis he distinguished the disorder from "**démenceprécoce**" (**schizophrenia**) and used the term '**manic depressive psychosis**' to describe it. **Kraepelin** emphasized that, in contrast to **démenceprécoce**, manic depressive psychosis had an episodic course and a more compassionate outcome. Some psychiatrists and some people with bipolar disorder still prefer the term '**manic-depressive illness**' because they feel that it reflects the nature of the disorder more accurately.

But Kraepelin could **not distinguish** between people with **both manic and depressive episodes** and people with only **depressive episodes with psychotic symptoms**. Trying to find out this **distinction** is largely responsible for the modern emphasis on **bipolarity**, and on **mood elevation** which help in defining the feature of the bipolar disorder.

1.4 Signs and Symptoms of bipolar disorder: [15-18]

- i. **Volatile Mood or Mood Swing:** Bipolar disorder can be clarified the rapid & frequent changes of mood episodes in one's. The mood change occurs at a time interval. The time

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interval may be specified for someone but it is non-specified in most cases. Sometimes the mood change occurs on certain circumstances or incidence.

- ii. Depression:** As a human being most people have low moods due to some difficulties or disappointment in life or due to other factors. Because it is hard to find a human being who is upbeat all of the time. It is not possible for any human being to be satisfied in all spares of life so having a low mood is a normal phenomenon for human beings. But having excessive low mood frequently is an abnormal phenomenon which leads a person to **depression**. Gradually this depression develops bipolar disorder in one's.
- iii. Euphoria:** The opposite portion of having low mood is having euphoria. So person with bipolar disorder is seen to euphoric for the time being. They have such energy levels that they don't feel any need to sleep nor eat. They may be constantly talking and overflowing with self-confidence. They are likely to involve themselves in all kinds of activities without thinking too deeply. They try to perform energetically in all activities with efficiency. But almost instantly this upbeat mood is transformed into a depression.
- iv. Hallucination:** Sometimes people with bipolar disorder lose their perception on reality. They might think police are looking for them to arrest for an imaginary crime, or they might think themselves of famous personality, or they might hear imaginary sounds or think different imaginary characters. Some of them claim to be possessed of some special psychic power or super natural power. But this hallucinating state doesn't exist them constantly, after a certain time the sufferer appears perfectly normal. Moreover hallucination occurs at a certain episode of mood swing.
- v. Substance Abuse:** Bipolar disorder of a person increases by involving in substance abuse. Alcohol and drugs seem to offer quick fixes or escapes from black thoughts, difficulties in relationships and the low self esteem that accompanies this condition. Moreover the strong appeal for the addicting substance worsens his/her mood stability which leads to the severe stage of bipolar disorder.
- vi. Creativity:** The person suffering from bipolar disorder these would be some periods of intense creativity. In some extent, they have a quality of thought and expression that might find an outlet in art, literature or some other creative field. If they can successfully challenge their inspiration into such activities they may achieve a great deal, but the phases of mood swing returns them to their normal selves or plunges them into a manic depression where all their creativity vanishes.
- vii. Suicidal feelings:** Often people with bipolar disorder live in an extreme depressive state. They start to think that their lives have no value and thus suicidal thinking arises in his/her mind. This feeling of suicides is induced the depression in a severe condition which bringing up the suicidal tendency in a person with bipolar disorder.

- viii. Varied mood swing patterns:**The mood changes in bipolar disorder occur in some patterns. Some people experience dramatic swings from high to low moods without any normal intervals in between while others do go through what family and friends consider as conscientious periods between their lows and highs. In other cases sufferers shows the signs of depression combined with the manic energy at a same time that characterizes a mood upswing. In some cases upswings occur more often than the downswings or vice versa. The severity of symptoms is also very much an individual matter with the lightest cases classified as cyclothymia rather than bipolar disorder.
- ix. Eccentricities:** In many cases people with bipolar disorders lay behind their eccentricity. Those with this condition may throw aside all normal social conventions to behave in the strangest of ways, or they dress in very bright colors or do other things that make them stand out from the crowd. Some people laugh or cry without any reason, some of them dance at any time, at any place. In a word they behave in a very abnormal way.
- x. Tiredness:** Executive function is the voice inside one’s head that gives a person the motivation to do daily tasks and concentrate on making decisions. People who are depressed often exhibit signs of executive *dys*function. It is difficult for them to plan, initiate, or complete tasks. They find it incredibly hard to do even the most basic activities of daily living, such as taking out the garbage, washing the dishes, talking on the phone, or paying bills. Gradually they become lethargic.
- xi. Irritability:** Person with bipolar disorder day by day has experiencing that everything & every person annoying him/her. He/ she can’t tolerate any person surrounding him/her. It is a severe state of bipolar disorder.
- xii. Sleeping Disorder:** Some people sleep too little when they're depressed, and others sleep too much. Sleep disturbance is a classic sign of bipolar disorder and the key to recognizing it is to notice the change in one’s personal sleeping patterns. Physically and mentally fit people normally sleep well through the night, but a person with bipolar disorder notices that he/she often waking up and unable to get back to sleep, for which he/she worrying about sleep loss that leads to depression. If a person normally require less sleep and finds himself/herself sleeping for longer periods of time, having trouble getting out of bed, or still feeling exhausted after he/she had a full night’s sleep, this is also a red signs of bipolar disorder.
- xiii. Eating Disorder:** Many people eat excessively when they are sad or stressed. But people with severe bipolar disorder often have no interest in food or their health.

Because unstable state of mood makes food less appealing and he/she loses interest in eating food even though it is necessary.

- xiv. Feel of pain:** Pain can make one depressed, and depression can make one to feel pain. Studies show that those who suffer with chronic pain have three times the average risk of developing psychiatric symptoms, and those who suffer from depression have three times the average risk of developing chronic pain.
- xv. Social Phobia:** Social isolation is a clear sign of severe bipolar disorder, especially if it's exhibited clearly by someone who used to be outgoing and had a lot of vigor. Even though someone who is depressed often wants to hide from everyone, it's the last thing that they need because isolation breeds depression, and depression deepens isolation. Some people with bipolar disorder become irritated by the surrounding people for which they want to be isolated from the society.
- xvi. Lack of concentration:** Person of bipolar disorder faces difficulties to concentrate on any task because of changing his/her mood into different phases frequently.

1.5 Drugs used in bipolar disorder:

Some major drugs that are used in the treatment of bipolar disorder are as follows: [19-21]

- **Clonazepam:** It is anxiolytics, sedatives anticonvulsants. It is used for several types of seizures, including myotonic or atonic seizures, photosensitive epilepsy, and absence seizures, although tolerance may develop. It is seldom effective in generalized tonic-clonic or partial seizures. The mechanism of action appears to involve the enhancement of gamma-aminobutyric acid receptor responses. Its primary mode of action is to facilitate GABAergic transmission in the brain by a direct effect on benzodiazepine receptors.
- **Procyclidine:** An Antimuscarinic drug. It is a muscarinic antagonist that crosses the blood-brain barrier and is used in the treatment of drug-induced extrapyramidal disorders and in parkinsonism.
- **Sodium Valproate+ Valproic Acid:** Mood stabilizer. It may act by increasing gamma-aminobutyric acid levels in the brain or by altering the properties of voltage dependent sodium channels. Typically supplied in the sodium salt form.
- **Risperidone:** It is a benzisoxazole derivative, is an atypical antipsychotic drug with high affinity for 5-hydroxytryptamine (5-HT) and dopamine D2 receptors. It is useful in treating schizophrenia including affecting symptoms. And also other psychotic conditions where positive and/or negative symptoms are prominent owing to its affinity for its "loose" binding

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affinity for dopamine D2 receptors and additional 5-HT antagonism compared to first generation antipsychotics, which are strong, non-specific dopamine D2 receptor antagonists. It reduces behavioral disturbances, activity disturbances.

- **Pregabalin** :AnAnxiolytics, Sedatives and anticonvulsants. Pregabalin subtly reduces the synaptic release of several neurotransmitters, apparently by binding to alpha2-delta subunits, and possibly accounting for its actions in vivo to reduce neuronal excitability and seizures. It is also used to treat peripheral and central neuropathic pain, generalized anxiety disorder and post herpetic neuralgia.
- **Busprione** :An anxiolytic agent. It displaces 8- OH-DPAT from 5-HT1A receptor binding sites, in addition to some D2 receptor antagonist activity. 8-OH-DPAT is an aminotetraline derivative that is a selective agonist for the 5-HT1A receptor. The first reports on 8-OH-DPAT were structure-activity studies showing that 8-OH-DPAT is devoid of dopaminergic activity, whereas compounds with a hydroxy group in various other positions of the aromatic ring of aminotetralines have substantial dopaminergic activity. This 8-OH-DPAT is selective for the 5-HT_{1A} receptor, 8-OH-DPAT was later found to act as serotonin reuptake inhibitor/releasing agent. Busprione displace this from 5-HT1A receptor and stimulates the receptor on nerves and alter chemical messages that nerves transmit to each other. Thus it works as an anxiolytic agent.
- **Oxcarbazepine**: An anticonvulsant used to control **grand malseizures** (a **loss of consciousness and violent muscle contractions**) and **psychomotor or focal seizures**. Its Mode of action:
 - ✓ Blockade of Na⁺ channels
 - **Reduces the propagation of abnormal impulses in the brain**
 - **Inhibit the generation of repetitive action potential**
 - ✓ Inhibit the release of glutamate
- **Quetiapine**: It is a second-generation antipsychotic that has affinity for D2, 5-HT2A, H1, alpha 1 and 5-HT1A receptors. Its precise mechanism of action is unknown, but according to the dopamine theory of schizophrenia, antipsychotic effects might be related to the drug's ability to reduce dopaminergic neurotransmission in the mesolimbic pathway.
- **Olanzapine** : It is a second-generation antipsychotic that acts as antagonist at 5HT2A and D2 receptors. The mechanism of action of olanzapine, as with other drugs having efficacy in schizophrenia, is unknown. However, it has been proposed that this drug's efficacy in schizophrenia is mediated through a combination of dopamine and serotonin type 2 (5HT2) antagonism. The mechanism of action of olanzapine in the treatment of acute manic or mixed episodes associated with bipolar I disorder is unknown.

- **Carbamazepine** :It is a tricyclic compound chemically related to tricyclic antidepressants (TCA) with anticonvulsant and analgesic properties. Carbamazepine exerts its anticonvulsant activity by reducing polysynaptic responses and blocking post-tetanic potentiation. Its analgesic activity is not understood; however, carbamazepine is commonly used to treat pain associated with trigeminal neuralgia. It depresses thalamic potential and bulbar and polysynaptic reflexes.
- **Tramadol HCL** :It exerts its analgesic effect by two ways an opioid effect and an enhancement of serotonergic and adrenergic pathways. It acts on the central nervous system.
- **Aripiprazole**: It is a partial agonist at D2 receptors. It may act as an antipsychotic by:
 - Lowering dopaminergic neurotransmission in the mesolimbic pathway.
 - Enhancing dopaminergic activity in the mesocortical pathway.
- **Quetiapine fumarate**: It is a **psychotropic agent** belonging to the chemical class of benzisoxazole derivatives and is indicated for the treatment of schizophrenia. Quetiapine fumarate is a selective monoaminergic antagonist with high affinity for the serotonin Type 2 (5HT₂), and dopamine type 2 (D2) receptors. Quetiapine fumarate is an antagonist at serotonin 5-HT_{1A} and 5HT₂, dopamine D1 and D2, histamine H1, and adrenergic alpha 1 and alpha 2 receptors. Quetiapine fumarate has no significant affinity for cholinergic muscarinic or benzodiazepine receptors. Drowsiness and orthostatic hypotension associated with use of quetiapine may be explained by its antagonism of histamine H1 and adrenergic alpha 1 receptors, respectively.

1.6 Abusive drugs:

According to this study, the **major** drugs that are abused by the patient of bipolar disorder [22-24]

Benzodiazepine:

- is the chief inhibitory neurotransmitters in the C.N.S
- counteracts the effects of glutamate
- via the uptake of negatively charged chloride ions to pass through the postsynaptic neuron
- hence post synaptic neuron less responsive to excitatory neurotransmitters

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- Thus GABA has a sedative (tranquilizing effect) on the brain. So, intake of it properly can be the short term solution for sleep problems, anxiety, stress reactions like panic attack and muscle spasms. But taking this in an appropriate amount causes tolerance and dependency on it which termed as addiction.

Methamphetamine:

It causes one's brain to **release excess Dopamine**. Dopamine is a chemical that gives negative feelings. It is the part of the reward mechanism in the brain. The receptors for dopamine shut down after prolong exposure to high levels of dopamine. Thus causes damage to the reward centers in the brains of **Methamphetamine users**.

Cannabinoids:

It produces a euphoria or 'high' in the user that's why it is taken as recreational .use. it includes a feeling of intoxication, with decreased anxiety, alertness, depression and tension and increased sociability (if taken in friendly surroundings). The overwhelming reason for taking cannabis given by recreational users is simply 'pleasure'

Cannabinoids act on brain reward processes and reward-related behaviors in strikingly similar fashion to other addictive drugs.

- **they enhance the electrical brain-stimulation reward in the reward circuitry of the brain**
- **they enhance neural firing of a core dopamine (DA) component of reward regulatory circuit**

1.7 Statistics:

Bipolar disorder is a disease that typically begins in early adulthood; between the ages of 15 and 25. Men tend to get develop bipolar disorder slightly earlier than women; whereas most males become ill between 16 and 25 years old, most females develop symptoms between ages 25 and 30. The average age of onset is 18 in men and 25 in women. bipolar disorder onset is very rare for people under 10 years of age, or over 40 years of age. (Source: The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Cambridge, MA: Published by the Harvard School of Public Health on behalf of the World Health Organization and the World Bank, Harvard University Press, 1996.)

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- The Prevalence Rate for bipolar disorder is approximately 1.1% of the population over the age of 18 (source: NIMH) or, in other words, at any one time as many as 51 million people worldwide suffer from bipolar disorder, including;
 - 12 million people in China
 - 8.7 million people in India
 - 2.2 million people in USA
 - 285,000 people in Australia
 - Over 280,000 people in Canada
 - Over 250,000 diagnosed cases in Britain
 - Rates of bipolar disorder are very similar from country to country—about 1 percent of the population.

Another way to express the prevalence of bipolar disorder at any give time is the number of individuals affected per 1,000 total population. In the United States that figure is 7.2 per 1,000. This means that a city of 3 million people will have over 21,000 individuals suffering from bipolar disorder.

Incidence: The number of people who will be diagnosed as having bipolar disorder in a year is about one in 4,000. So about 1.5 million people will be diagnosed with bipolar disorder this year worldwide. About 100,000 people in the United States will be diagnosed with bipolar disorder this year.

Prevalence of bipolar disorder compared to other well-known diseases

The term 'prevalence' of bipolar disorder usually refers to the estimated population of people who are living with bipolar disorder at any given time. The term 'incidence' of bipolar disorder refers to the annual diagnosis rate, or the number of new cases of bipolar disorder diagnosed each year. Therefore, the approximate number of people in the United States suffering from:

- bipolar disorder: 2.2 million people
- Multiple Sclerosis: 400,000 people
- Insulin-dependent Diabetes: 350,000 people
- Muscular Dystrophy: 35,000 people

The Course of bipolar disorder

- Early intervention and early use of new medications lead to better medical outcomes for the individual
- The earlier someone with bipolar disorder is diagnosed and stabilized on treatment, the better the long-term prognosis for their illness
- Teen suicide is a growing problem -- and teens with bipolar disorder have a 50% risk of attempted suicide
- In rare instances, children as young as five can develop bipolar disorder.
- Anti-psychotic medications are the generally recommended treatment for bipolar disorder. If medication for bipolar disorder is discontinued, the relapse rate is about 80

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percent within 2 years. With continued drug treatment, only about 40 percent of recovered patients will suffer relapses. (Source: NIMH)

Wide variation occurs in the course of bipolar disorder. Some people have psychotic episodes of illness lasting weeks or months with full remission of their symptoms between each episode; others have

fluctuating course in which symptoms are continuous but rise and fall in intensity; others have relatively little variation in the symptoms of their illness over time. At one end of the spectrum, the person has a single psychotic episode of bipolar disorder followed by complete recovery; at the other end of the spectrum is a course in which the illness never abates and debilitating effects increase. (Source: OpenTheDoors). Recent research increasingly shows that the disease process of bipolar disorder gradually and significantly damages the brain of the person, and that earlier treatments (medications and other therapies) seem to result in less damage over time (source: UCLA NeuroImaging Lab)

After 10 years, of the people diagnosed with bipolar disorder:

- 25% Completely Recover
- 25% Much Improved, relatively independent
- 25% Improved, but require extensive support network
- 15% Hospitalized, unimproved
- 10% Dead (Mostly Suicide)
- After 30 years, of the people diagnosed with bipolar disorder:
 - 25% Completely Recover
 - 35% Much Improved, relatively independent
 - 15% Improved, but require extensive support network
 - 10% Hospitalized, unimproved
 - 15% Dead (Mostly Suicide)

(Source: Surviving bipolar disorder)

The area of existence of people with bipolar disorder:

Approximately:

- 6% are homeless or live in shelters
- 6% live in jails or prisons
- 5% to 6% live in Hospitals
- 10% live in Nursing homes
- 25% live with a family member
- 28% are living independently
- 20% live in Supervised Housing (group homes, etc.)

(Source: Surviving bipolar disorder)

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Homelessness and bipolar disorder

- Approximately 200,000 individuals with bipolar disorder or manic-depressive illness are homeless, constituting one-third of the approximately 600,000 homeless population (total homeless population statistic based on data from Department of Health and Human Services). These 200,000 individuals comprise more than the entire population of many U.S. cities, such as Hartford, Connecticut; Charleston, South Carolina; Reno, Nevada; Boise, Idaho; Scottsdale, Arizona; Orlando, Florida; Winston Salem, North Carolina; Ann Arbor, Michigan; Abilene, Texas or Topeka, Kansas.
- At any given time, there are more people with untreated severe psychiatric illnesses living on America's streets than are receiving care in hospitals. Approximately 90,000 individuals with bipolar disorder or manic-depressive illness are in hospitals receiving treatment for their disease.
(Source: Treatment Advocacy Center)

The Cost of bipolar disorder to Society:

Bipolar disorder, long considered the most chronic, debilitating and costly mental illness, now consumes **a total of about \$65 billion a year** for direct treatment, societal and family costs. Richard Wyatt, M.D., chief of neuropsychiatry, National Institutes of Mental Health, has said that nearly 30 percent (\$19 billion) of bipolar disorder's cost involves direct treatment and the rest is absorbed by other factors -- lost time from work for patients and care givers, social services and criminal justice resources.

Wyatt said bipolar disorder affects one percent of the population, accounts for a fourth of all mental health costs and takes up one in three psychiatric hospital beds. Since most bipolar disorder patients are never able to work, they must be supported for life by Medicaid and other forms of public assistance. (Source: NIMH)

A more recent estimate of the cost of bipolar disorder and other serious mental illnesses (bipolar disorder, serious depression, etc) from Dr, E. Fuller Torrey in Q1, 2004 was that federal costs for the care of seriously mentally ill individuals now total **\$41 billion yearly** and are rocketing upward at a rate of \$2.6 billion a year.

More hospital beds in Canada (8%) are occupied by people with bipolar disorder than by sufferers of any other medical condition (Source: BCSS)

In the UK, in economic terms: some 80 million working days are lost each year at a cost of £3.7 billion; the NHS spends around £1 billion on treatment and personal social services another £400 million.

The greatest cost of bipolar disorder , however, is the non-economic costs to those who have it and their families.

Bipolar disorder Research Expenditures:

Research expenditures on bipolar disorder still lag far behind those on other serious illnesses. US Government spending on research per person - Comparison (For More information: [A Federal Failure in Psychiatric Research](#), November, 2003)

Disease	FY 1999 NIH research expenditures	Prevalence: Individuals with this disease	NIH research dollars per person affected
HIV (including AIDS)	\$1,792,700,000	800,000	\$2,240.88
lung cancer	\$163,100,000	342,457	\$476.26
cervical cancer	\$75,200,000	231,064	\$325.45
multiple sclerosis	\$96,300,000	350,000	\$275.14
breast cancer	\$474,700,000	2,197,504	\$216.02
colorectal cancer	\$175,900,000	1,041,499	\$168.89
Parkinson's disease	\$132,300,000	1,000,000	\$132.30
prostate cancer	\$177,500,000	1,637,208	\$108.42
Alzheimer's disease	\$406,500,000	4,000,000	\$101.62
bipolar disorder	\$196,515,000	2,632,396	\$74.65
bipolar disorder	\$57,805,000	2,227,412	\$25.95
depression	\$199,600,000	10,732,076	\$18.60
panic disorder	\$19,049,000	3,239,872	\$5.88
obsessive-compulsive disorder	\$12,693,000	4,859,808	\$2.61

NIH Research Expenditure by Disease, 1999

Suicide Risk

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People with the condition have a 50 times higher risk of attempting suicide than the general population; the risk of suicide is very serious in people with bipolar disorder. Suicide is the number one cause of premature death among people with bipolar disorder, with an estimated 10

The Risks of Getting bipolar disorder

After a person has been diagnosed with bipolar disorder in a family, the chance for a sibling to also be diagnosed with bipolar disorder is 7 to 9 percent. If a parent has bipolar disorder, the chance for a child to have the disorder is 10 to 15 percent. Risks increase with multiple affected family members.

1.8 Aim and Objective:

There is some **major** aims and objectives of this study such as follows:

- Determination of the approximate range of drug abuse in bipolar disorder in Bangladesh and non drug abuse in spite of having bipolar disorder
- Determination of the ratio of male & female involve in illicit drug abuse and having bipolar disorder.
- Mark the age group of people with bipolar disorder which is susceptible of taking different illicit drugs
- Clarify the most indicating signs and symptoms of people in bipolar disorder according to the perspective of Bangladeshi Doctors, Physicians and Psychiatrists .
- Receive an idea about the major illicit drugs that are taken by the people of bipolar disorder for being addicted.
- Clarify the chance of having bipolar disorder by checking out the patients' Family History.
- Determine the ratio of being involved in substance abuse with the longevity of this disorder.
- Finding out the causative reason of having bipolar disorder according to the circumstances of patient.
- Clarify the type of family bonding of the person with bipolar disorder but being involved in drug abuse

percent to 13 percent killing themselves and approximately 40% attempting suicide at least once (and as much as 60% of males attempting suicide). The extreme depression and psychoses that can result due to lack of treatment are the usual causes. These suicides rates can be compared to the general population, which is somewhere around 0.01%. (source: Treatment Advocacy Center and other sources)

Acknowledgement of mostly prescribing drugs given by the Bangladeshi Doctors to treat the patients with bipolar disorder who are involved in taking of illicit drug.

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Chapter-2

Literature Review



All around the world bipolar disorder is considered as a major concern. For which many Scientist, Researchers, Physicians work on different issues related to bipolar disorder. As like, some research works are mentioned here based on some issues that are connected to bipolar disorder:

Perugi G, Vannucchi G, Bedani F, Favaretto E had studied that use of stimulants in Bipolar Disorder. According to this study the stimulants, including methylphenidate (MPH), amphetamines and derivatives, modafinil, and armodafinil indicate stimulants, including methylphenidate (MPH), amphetamines and derivatives, modafinil, and armodafinil are indicated as second-third-line choices for bipolar depression indicated by several international guidelines. It is reported that stimulants are effective for the management of residual depressive symptoms such as fatigue and sleepiness and for the management of affective, cognitive, and behavioral symptoms in children and adult bipolar patients. But recently it has been reported that potential of misuse and abuse of these stimulants causes mood destabilization for which induction of (hypo) manic switches, mixed states, and rapid cycling occur. [25]

Cheniaux , Silva RAD, Santana CM, Filgueiras had studied on the “Changes in energy and motor activity: core symptoms of bipolar mania and depression”. They found that higher level of energy or activity in a person should be considered a core symptom of mania. They also found that Hamilton Depression Scale (HAM-D) probably does not assess motor activity adequately. [26]

Joint analysis of cognitive and circadian variation in Schizophrenia and Bipolar I Disorder had studied by the authors named Thomas, Mazumdar, Wood , Bhatia etc. They said that clusters based on levels of cognitive function can discriminate schizophrenia (SZ) patients from control individuals but not bipolar-I patients. Composite scale of morningness (CSM) scores does not contribute to such discrimination. [27]

Perich , Ussher , Parton had suggested that the mood changes during menopause of women through the lens of their existing framework of bipolar disorder, with implications for understanding of self and treatment choices. [28]

The mothers' prenatal exposure to lithium or mood disorders has no significant association with the offspring's IQ of children. This study was done by Forsberg, Adler. [29]

Predictors of suicide ideation among older adults with bipolar disorder was studied by Heisel , Canham. The significant predictors of suicide ideation were the young adults with bipolar disorder due to alcohol misuse and medication non-adherence. But in older adults with bipolar disorder cognitive failures directly and indirectly predict suicide ideation. [30]

Dols, Schouws had studied on Older patients with a bipolar disorder, considering them as a distinctive group and compared these findings with the research done in younger patients or older patients from the United States. As recommendations can't be extrapolated to older adults with bipolar disorders they stated that more research is needed to provide evidence based guidelines for this special population.[31]

Iversen, Steen said that the use of antipsychotics, and polypharmacy induce a high occurrence of symptoms in the patients with psychotic disorders. They also reported that due to the use of antipsychotics, and polypharmacy female gender are seemingly risk factors for reporting a severe side effect burden. [32]

Zhang & Wang stated that bipolar I patients followed motor suggestions more often under hypnosis which indicates the association between mania levels and certain hypnotic susceptibility features. This study performed for the better understanding the altered conscious states in bipolar disorders, and also for encouraging the use of related psychotherapy for these patients. [33]

Leclerc, Mansur had studied on the “differential association between history of childhood sexual abuse and the body mass index in early and late stages of bipolar disorder” , where they found that there is a relationship between childhood sexual abuse and BMI, but the direction of the association varies across the different stages of bipolar disorder-1. [34]

Kasahara ,& Kato had studied over the relationship between Mitochondrial DNA Analysis and Mood Disorders. On their study, they discuss about Mitochondrial DNA (mtDNA) analysis and also about neuropsychiatric disorders based on an example of Parkinson's disease. They stated about the challenges and future directions beyond Mitochondrial DNA (mtDNA) analysis toward an understanding of the pathophysiology of "idiopathic" mood disorders on that study.[35]

Zalsman shown on their study that except recurrent and familial disorder the depression among the children & adolescents is often accompanied by other comorbidities such as substance abuse, bipolar disorder, suicidal behavior and significant impairment. To rescue the children & adolescents from being grabbed by depression they suggested therapies include cognitive, interpersonal and pharmacological interventions. Recently, the FDA published a warning concerning the use of these pharmacological agents in the pediatric age group. [36]

Keskin & Tamam studied over the Assessment of sleep quality in bipolar euthymic patients. They describes on their study that poor sleep quality has a negative effect in euthymic episodes

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of bipolar disorder. For which they suggested that the assessment of sleep disturbances routinely through psychiatric interviews and dealing with sleep problems regardless mood episodes may improve sleep quality which improves functionality and quality of life. [37]

Gallur & Powell stated that it may be possible to recommence modified lithium therapy in older Adults with Bipolar I Disorder. This paper addresses considerations in recommencing lithium in elderly patients with Bipolar I Disorder and medical comorbidity. We focus on nephrotoxicity and cognitive impairment. Case reports and review of relevant literature proves that. According to it three elderly psychogeriatric inpatients admitted with severe manic relapse following lithium cessation are described. In all cases, lithium was recommenced safely with good response. Even with medical comorbidity it may be possible to recommence modified lithium therapy. [38]

Witusik & Pietras performed a qualitative analysis of the therapeutic process of a couple in which one partner suffers from bipolar affective disorder. They found throughout the study that bipolar disorder causes disturbances on marital functioning, the chances of occurring autism in their children related to the psychiatric disorders and the dysfunctionality of the parents with bipolar disorder. [39]

Weintraub & Van de Loo studied over the self harm tendency in adult patients with depression and bipolar disorder. According to their study Self-harm refers to the purposeful destruction of bodily tissue without suicidal intention and for purposes that are not socially sanctioned. They found in their study that the prevalence of lifetime self-harm was higher in patients with bipolar disorder in compare to the patients with a unipolar depressive disorder and this Self-harm was also more strongly linked to impulsivity in individuals with bipolar disorder compared with unipolar depressive disorder. [40]

Mishra , Krishna, Ramesh , Kishor had studied on the Impact of Pharmacist-Psychiatrist in the Patient Education on Medication Adherence and improvement of quality of life of bipolar disorder patient. Their study had shown that when pharmacists worked as a team with psychiatrists' patient education can significantly improve the medication adherence and quality of life (QOL) of the Bipolar Affective Disorder (BPAD) patients. [41]

Amini, Ghaleiha, Mahjub had studied over some patients with bipolar disorder in the west of Iran. They found in their study that mania was much more prevalent than depression and mixed episodes. They also reported that sex, treatment, and season can determine the episodes of bipolar disorder. [42]

Holtzman , Kenna, Rasgon stated on their study that intake of Lamotrigine and GABAA receptor modulators interact with menstrual cycle phase and oral contraceptives which regulate mood in women with bipolar disorder. They showed that the fluctuation of mood during menstruation occurs so frequently in women with bipolar disorder than in the women of healthy control group. Intake of Lamotrigine and GABAA receptor modulator helps in regulating the mood of the female patients with bipolar disorder. [43]

Cherry, Braimoh, Lumley showed on their study that positive parenting has a positive impact on Psychopathology of Youth with a Diagnosis of Bipolar Spectrum Disorder. Along with treatment, positive parenting facilitates the steps of maintaining quality of life of the patient of bipolar disorder.[44]

Torres, Garriga, Sole had shown the range of functional impairment in adult patients of bipolar disorder who have ADHD (attention-deficit/hyperactivity disorder). From their study it is proved that, adult patients having both Bipolar Disorder (BD) & ADHD (attention-deficit/hyperactivity disorder) showed the worst scores in functioning compared with the healthy controls (HCs), but did not show more severe functional impairment than the pure bipolar disorder (pBD) group except for the cognitive domain. [45]

Taub, Feingold, Rehm had performed a study which reports that the range of using cannabis among the individuals with Major Depressive Disorder (MDD) and Bipolar Disorder (BPD). The result of the study indicates that individuals with BPD may present more intensive patterns of cannabis use in compare to those with MDD. [46]

Bhalla, Stefanovics, Rosenheck had done a study together where they showed the clinical epidemiology of single versus multiple substance use disorder. In this study, it is reported that the higher levels of Poly Substance Use Disorder (PSUD) develop schizophrenia, bipolar disorder, major depressive disorder, and personality disorders. Moreover, higher levels of Poly Substance Use Disorder (PSUD) are associated with greater use of psychiatric inpatient care, residential and rehabilitative treatment, and with multiple psychotropic medication prescription fills. [47]

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Perret , Fakra , Simon studied on alcohol use and bipolar disorder by observing two groups of sample one which have already Alcohol Use Disorder (AUD) & then developed Bipolar Disorder (BD) and the another group of sample which have Bipolar Disorder and after that alcohol use disorder (AUD) developed. From these two groups the first group (AUD- BD group) might have been used alcohol to reduce stress and tension caused by the presence of an irritable temperament as well as anxious and organic disorders, leading to first depressive episode. In the second group (BD-AUD group) use of alcohol works as a stimulant that might have triggered the first manic episode, and alcohol abuse result from mania severity. [48]

Williams, Davey-Rothwell, Latkin described about the health risk behaviors of the People Who Have Mood Disorders and use to Inject illicit Drugs. Through the study they stated that these injected illicit drugs worsen their mental health and increases the frequency of mood swing. [49]

Messer, Müller-Siecheneder, Latifi studied over the substance abuse in patients with bipolar disorder. In this study it is reported that many patient with bipolar disorder gradually being affected by any kind of substance use disorder (SUD) by involving themselves in substance abuse. But this SUD was not related to age, subtype of Bipolar Disorder (BD), hospitalization and co-existence of anxiety disorders or psychotic symptoms. Moreover it was shown that SUD increases the severity of BD in some cases and in some cases BD influences to be habituated in drug abuse. [50]

Maksimovskiy stated on his study that use of alcohol causes the cerebral cortex thinner and enlarge the ventricles which ultimately exert a severe negative effect in schizophrenia, **bipolar disorder**. Throughout the study they exemplify their statement by observing several groups of study sample. [51]

In Madrid there's a study performed by Arias, Szerman, Basurte on which they had shown the relationship between **bipolar disorder** and **substance use disorders**. Their study reported that the range of alcohol consumption and cocaine intake is higher in person with bipolar disorder than the non bipolar disorder. It is also reported that the person having bipolar disorder from childhood is being habituated alcohol intake at the very early age of life compared to other non bipolar alcoholics. [52]

Cardoso, Bauer, Jansen had described about the bad Effect of using alcohol and illicit substance by the individuals with bipolar disorder. Through this study they had shown that the habituation of substance abuse is associated with an earlier onset of bipolar disorder. [53]

Muneer had performed a study on Pharmacotherapy of Acute Bipolar Depression in Adults. The pharmacological agents that are used in the management of acute bipolar depression and their effects are briefly discussed on this study. To exemplify the study the author described divalproex sodium as a suitable mood stabilizers for acute depression while olanzapine, quetiapin ,lurasidone, and cariprazine, were described as atypical antipsychotics, which are also effective, in acute bipolar depression. [54]

Chapter-3

Materials and Method



3.1 Study Location: Dhaka

3.2 Places where study subjects were interviewed :

The places where the patients were searched for this study :

- four Drug Rehab centre
- two Counseling Centre
- one mental hospital

They are:

- **Drug Rehab Center :**

The rehab centre where the patient have been studied for this study purpose as follows :

<i>Name of Rehab Centre</i>	<i>Location</i>
Amar Home	Uttara
Bijoy	Uttara
Phera	Uttara
Promises	Baridhara J Block

- **Counseling Centre :**

The counseling centre where the patients were interviewed :

<i>Name of Counseling Centre</i>	<i>Location</i>
Mon Counseling Centre	Framgate
Manshuba Counseling Centre	Uttara

- **National Institute Of Mental Health (NIMH) :** It is situated at Mirpur Rd, Dhaka.

We have found total 200 patients.

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3.3 We have taken an interview orally as well with a written Questionnaire. Sample questionnaire is attached here with.

Research Questionnaires:

SI No.: Year: Month: Registration No. :

Hospital: Clinic: Institute:

Patient Info:

Age: Sex: Male Female Body Weight in Lbs:

Consultant: Specialized General Physician

Admission Diagnosis: Admission Date:

Final Diagnosis:

Additional Diagnosis:

Order of Recording:

1. Major Complaints:

2. Present Illness

3. Past History: General Exam Systemic Exam

4. Family History:

5. Socio- Economical Condition:

6. Drug Allergy:

Questions asked to the Patient:

1. From when you are suffering from bipolar disorder?
2. Is there is anybody in your family who has Bipolar Disorder?
3. According to your physician what are the causative reason of your bipolar disorder?
 - a. Family issue
 - b. Personal Relationship
 - c. Major Accident
 - d. Job insecurity
 - e. Others
4. How about your family bonding?
 - a. Excellent
 - b. Good Enough
 - c. Not that Good
 - d. Worse
5. How often you get violent when the symptom occurs?
 - a. Frequent
 - b. Sometimes
 - c. Rare
 - d. Never
6. How your family manages you when you get violent?
7. To overcome depression did you involve in taking any drug?
 - a. Yes
 - b. No
- 8 If yes than what are those substances?
 - a. Antidepressant drug
 - b. Alcohol
 - c. Smoking
 - d. Others
9. How often u consult your doctor?
10. What types of medicines are prescribed by your physician / doctor?

Drug Chart

Generic Name	Brand Name	Dosage Form & Strength	Dose	Route	Frequency	Duration

11. Do you take any sleeping pill for take a sleep at night? If take, then which tablet do you take for this?

12. Do you think substances that cause addiction are the best way to get relief from depression?

- a. Yes b. No

13. Do you have any job related depression?

- a. Yes b. No

14. Do you suffer from eating disorder or sleeping disorder or do you hallucinate something?

15. Do you face any symptoms when you withdraw your medications? Do you face any side effect during taking your medications?

- a. Yes b. No

16. Do you think to kill yourself ever?

- a. Yes b. No

17. Do you think your life is normal than before?

- a. Yes b. No

Chapter-4

Result and Discussion



4.1 Patient Numbers :

Total Patient=200

Drug Abuse in bipolar disorder = 60

Drug Abuse in Non Bipolar Disorder = 140

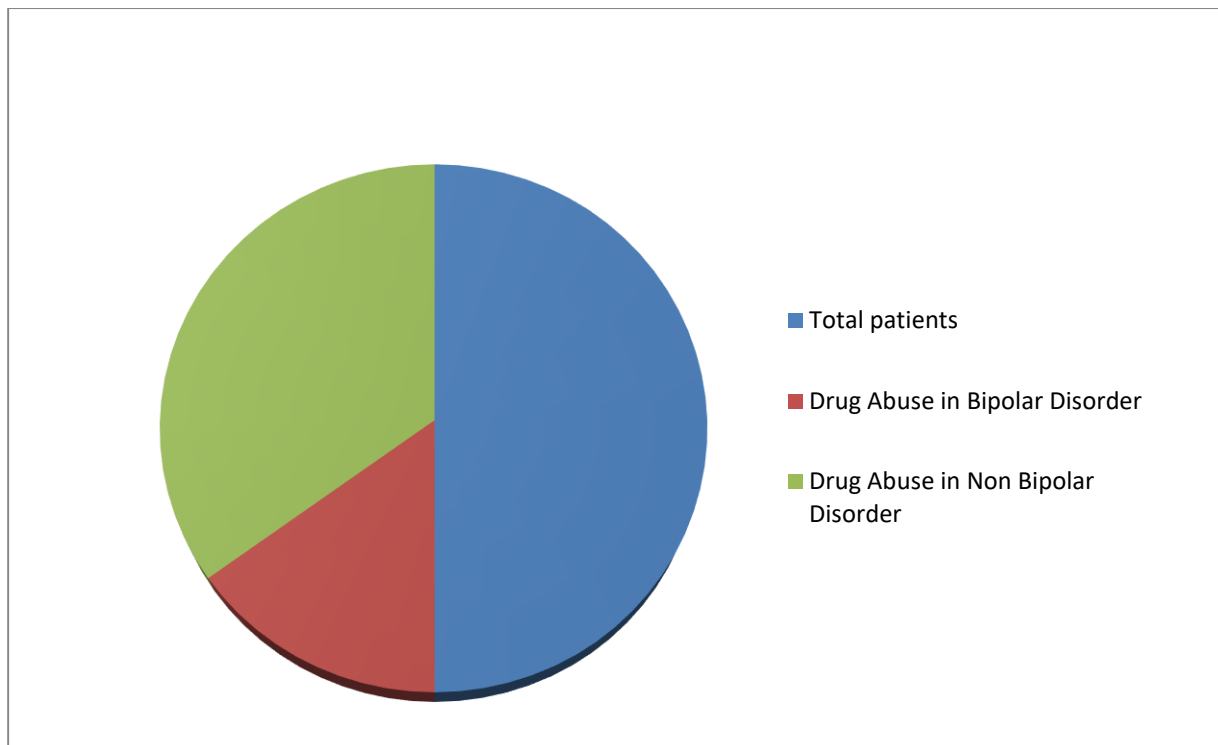


Figure 1.1: Total Number of patients, Drug abuse with bipolar disorder patients, and Drug abuse with non bipolar patients

From the graph it is seen that the total number of observed drug addicted patient is 200 among which we have found only 60 patients who have bipolar disorder but rest of 140 patients do not have bipolar disorder. So it can be said that in most cases bipolar disorder does not influence a person to involve in drug addiction . It may occur for few persons but their number is very minor.

4.2 Range of male & female patient:

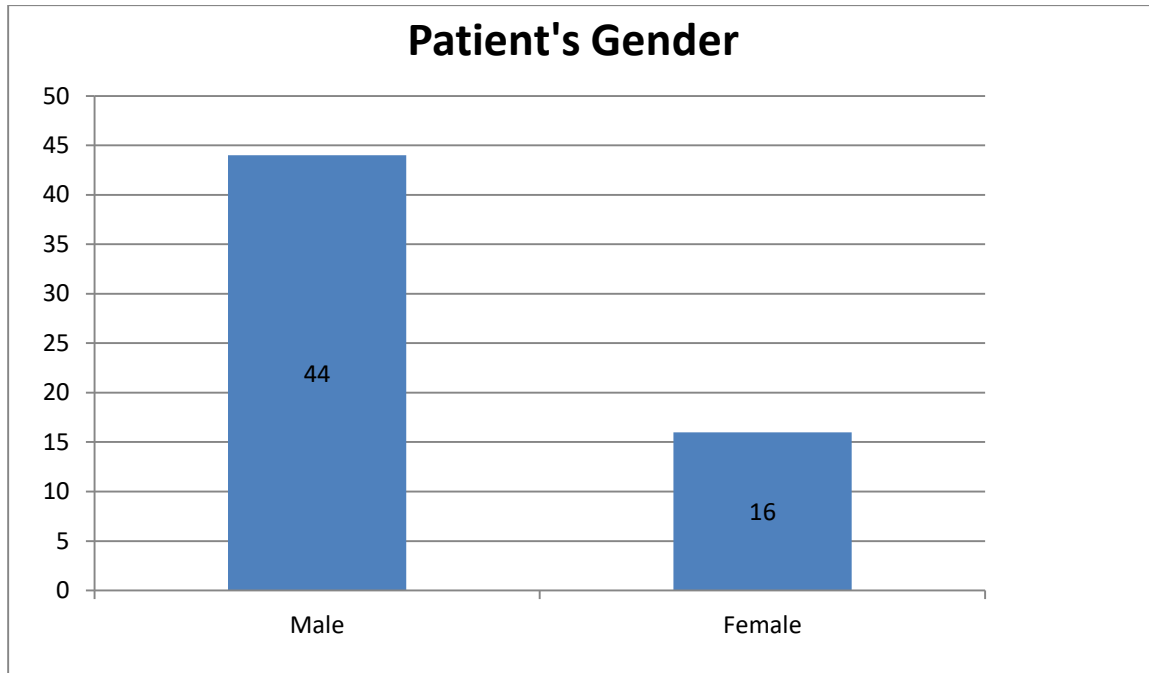


Figure 1.2: number of male and female patient of bipolar disorder with drug abuse

This graph is shown that the number of male drug addicted patient with bipolar disorder is higher in comparison to female drug addicted patient with bipolar disorder

4.3 Age Range of Patients:

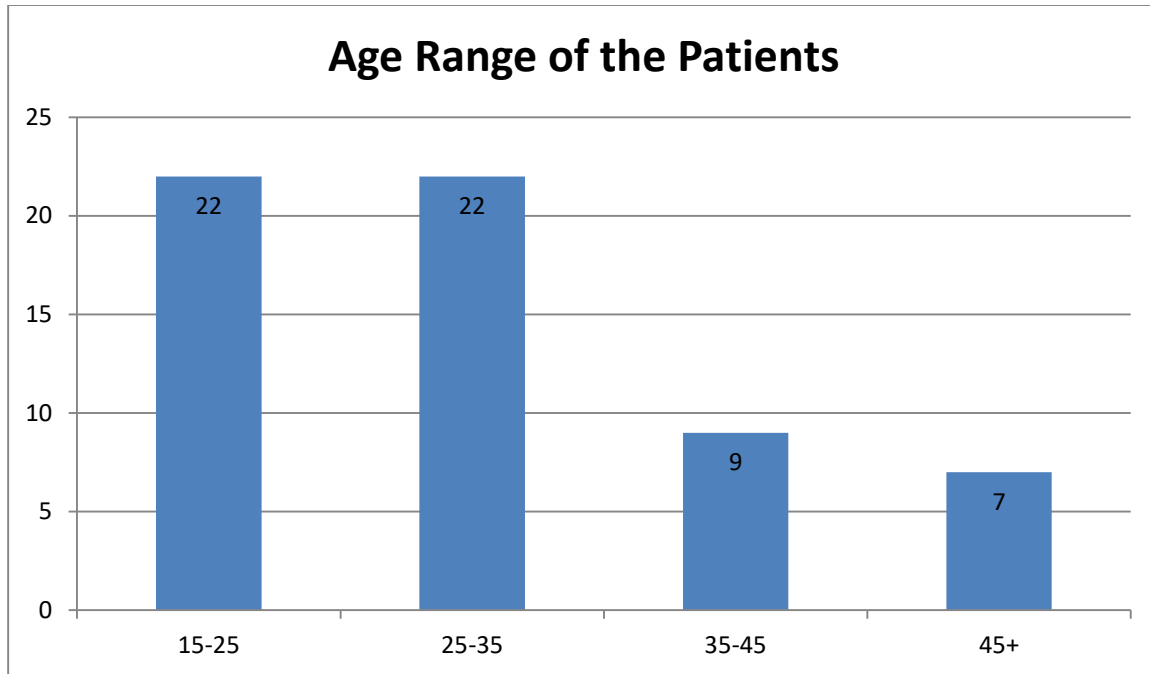


Figure 1.3: The susceptible age range of bipolar disorder patient of being drug addicted

Through this graph it is shown that the most vulnerable age groups patient of bipolar disorder is 15-25 years and 25-35 years for drug abuse. That means persons having bipolar disorder within the age of 15-35 years have the high chance of being addicted to drug than other age group of people.

4.4 Symptoms of patient found in admission diagnosis done in hospital or clinic or counseling centre or rehab centre:

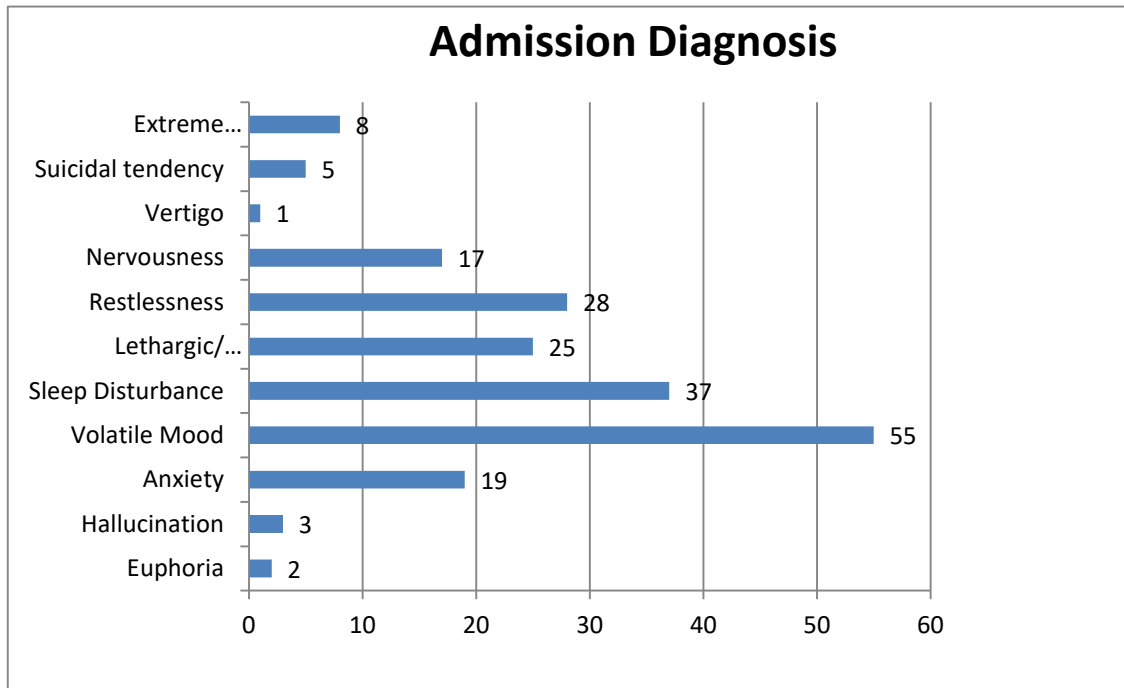


Figure 1.4: The symptoms of patients marked in the admission diagnosis in the Hospital / Rehab/ Counseling centre

This graph shows that in the admission diagnosis of the addicted patient with bipolar disorder, Volatile mood (mood swing), sleep disturbance, restlessness, anxiety are some common symptoms that are recorded.

4.5 Diagnosis of the presence of abusive drugs in the patients' Blood-Urine Test:

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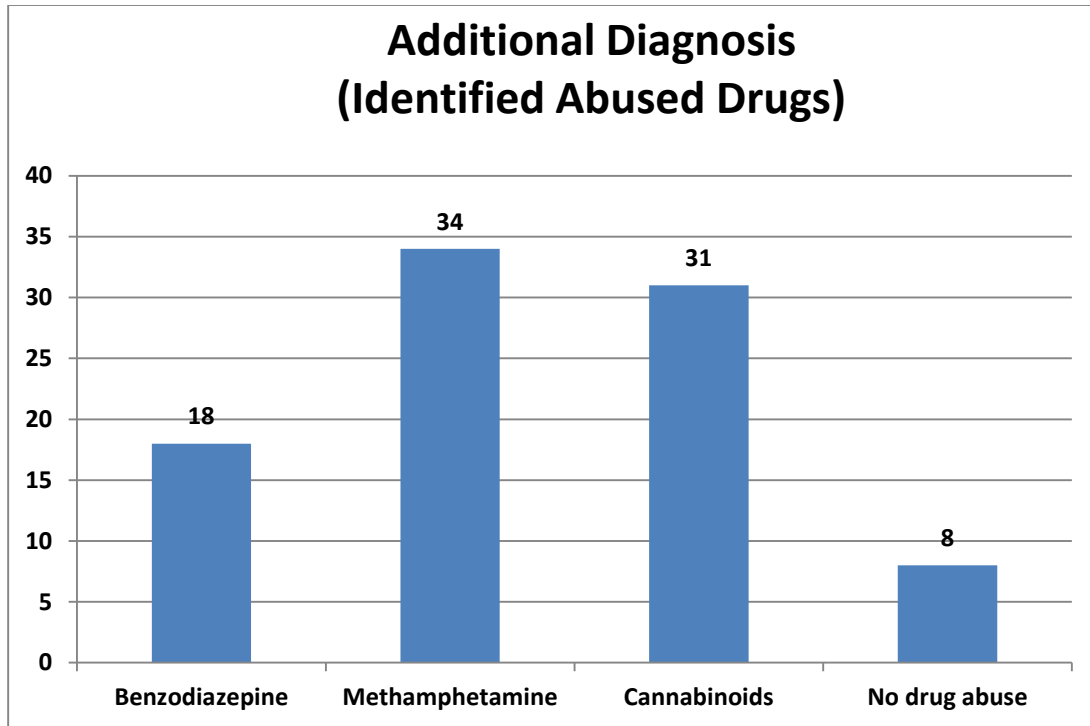


Figure 1.5: The mostly abusive drugs taken by the studied patents

This graph shows the percentage of using Benzodiazepine, Methamphetamine, Cannabinoids which are illicit drugs taken by the drug addicted -bipolar disorder patient. From this graph it can be shown that according to the circumstances of Bangladesh the availability of Methamphetamine is greater than the other illicit drugs for which most addicted persons prefer it for their stimulation.

4.6 The Major Complaints of family & relatives against the patient:

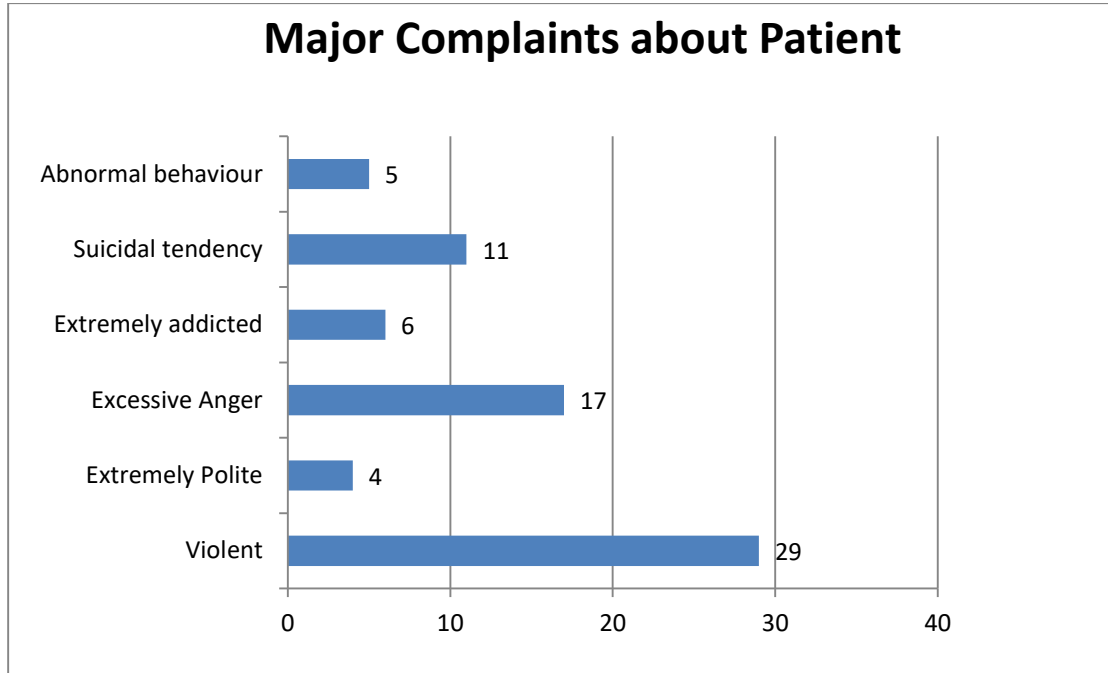


Figure 1.6: Complaints of the family & relative against the patient of drug addicted with bipolar disorder

The addicted patients who are suffering from bipolar disorder shows some unexpected behavior for which their families have complaints against them & try to give them better treatment under the supervision of specialized doctors, psychiatrists. Among their unexpected behavior being violent, having excessive anger, having suicidal tendency are most common major complaints against them that are found on this study.

4.7 Duration of having the bipolar disorder of the patient:

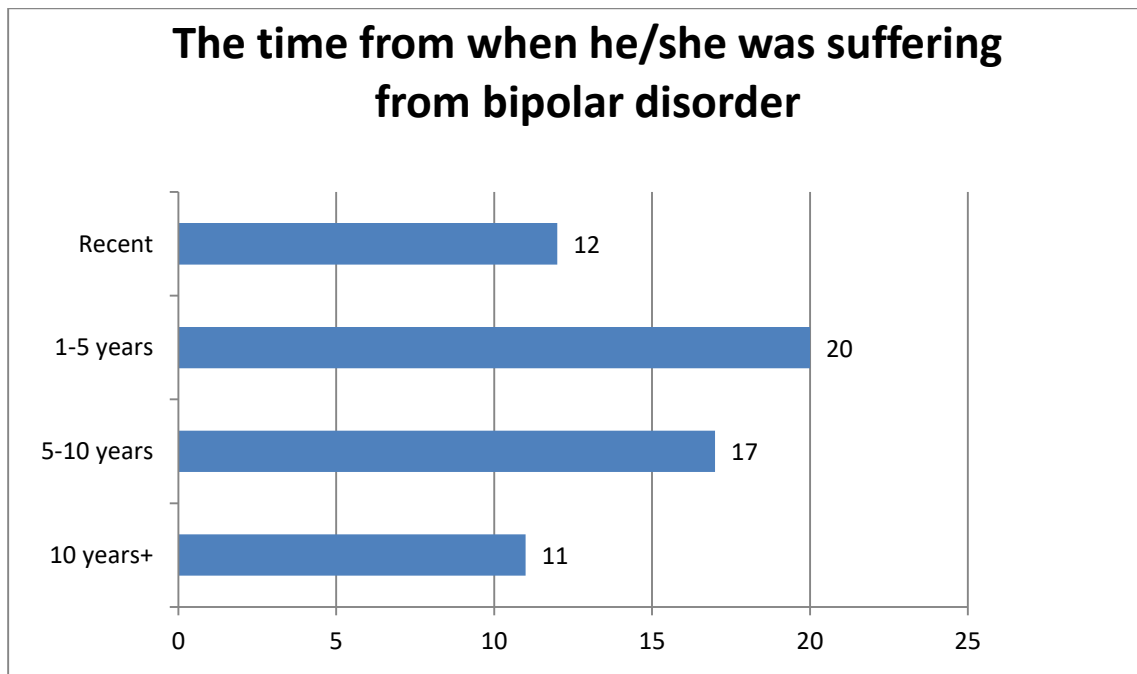


Figure 1.7: Duration of having the bipolar disorder of the studied patents

This graph is shown the duration of time from when the addicted patients suffer from bipolar disorder. From here we can see that in most cases the patients of bipolar disorder have been suffering from 1-10 years before undergo any medical treatment.

4.8 The family member of the patient having bipolar disorder

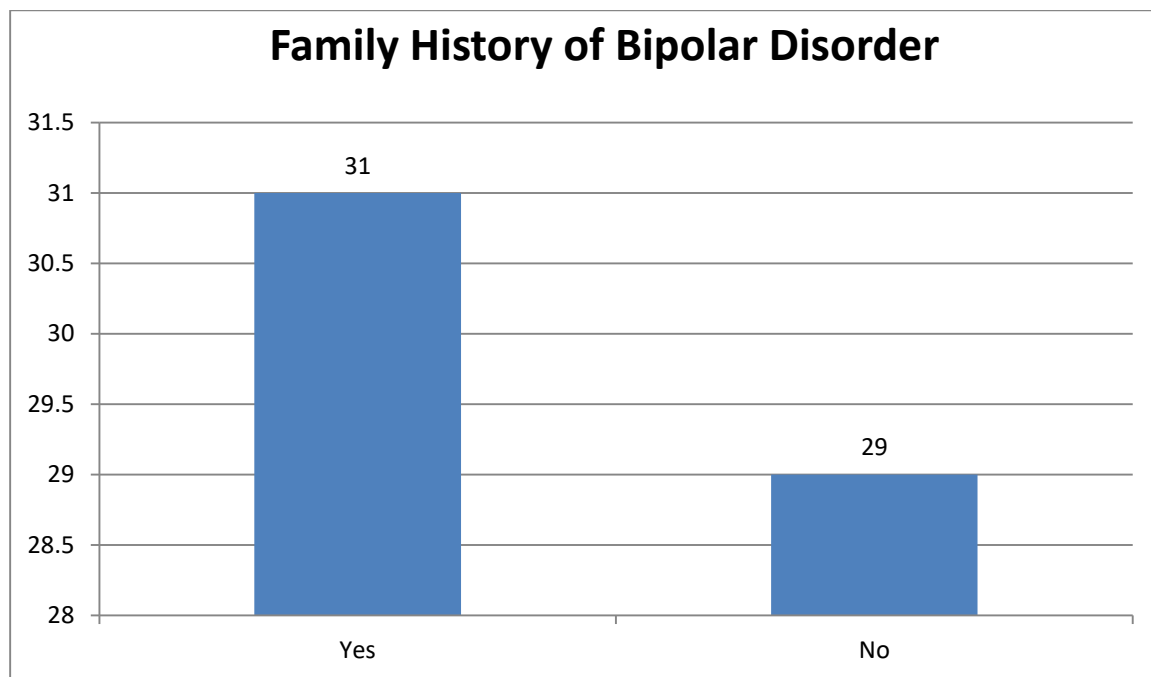


Figure 1.8: The family member of the patient having bipolar disorder

From this graph it is shown that family history of bipolar disorder is a major reason of having bipolar disorder. That means genetic factors play a vital role in spreading the bipolar disorder among the other upcoming generations of a specific family.

4.9 The reason of having the bipolar disorder of the studied patients:

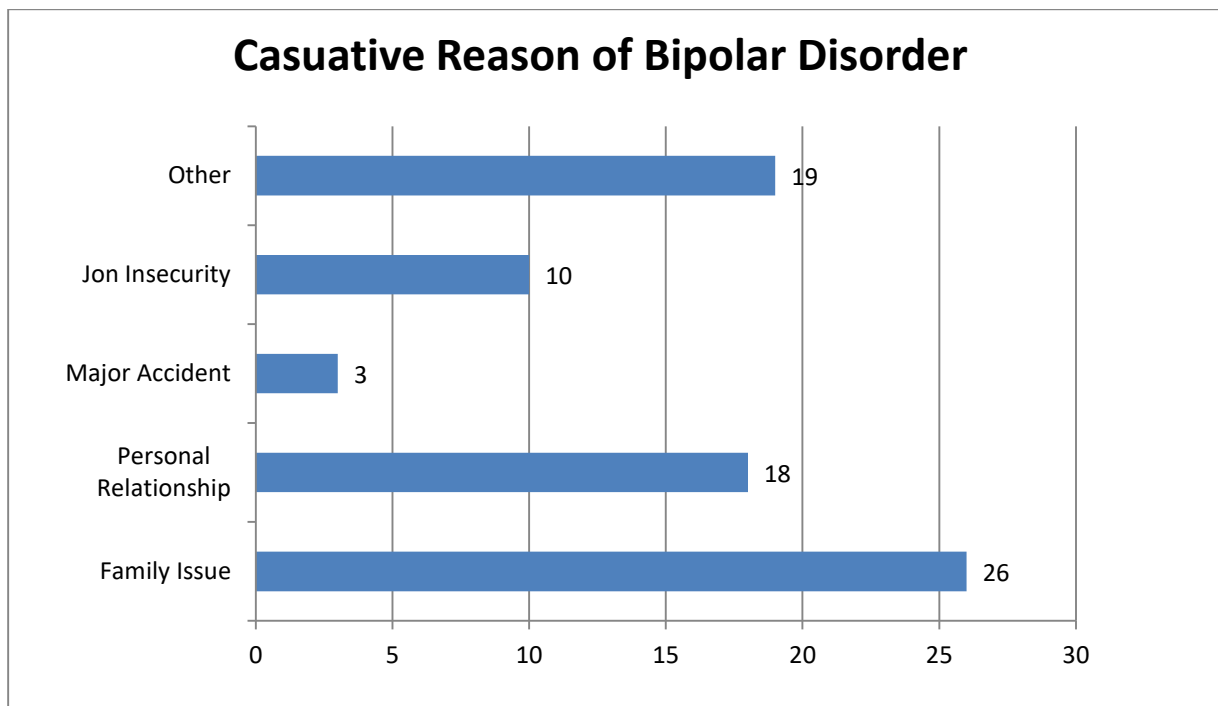


Figure 1.9: The causative reasons of having bipolar disorder of the studied patients

“A retrospective survey analysis on Drug Abuse in Bipolar Disorder on Bangladeshi population”

This graph is about the analysis of the reason of being affected bipolar disorder. Family issues, Personal Relationships are the most vital reasons than the other reasons.

4.10 Type bonding of the patient with his/her family:

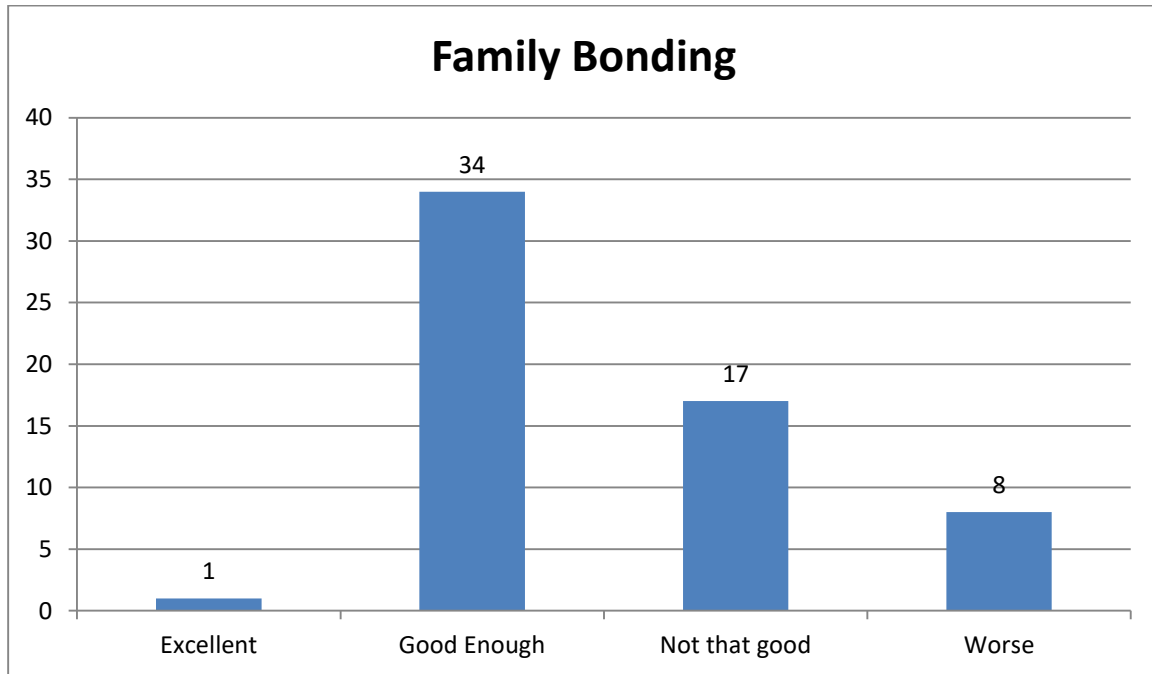


Figure 1.10: Type of bonding of the drug addicted bipolar disorder patient with own
Family

According to this graph, it can be shown that in spite of having a good relationship with family, a person with bipolar disorder has the chance of being addicted to illicit drugs.

4.11 Drugs administered for the patients that were studied:

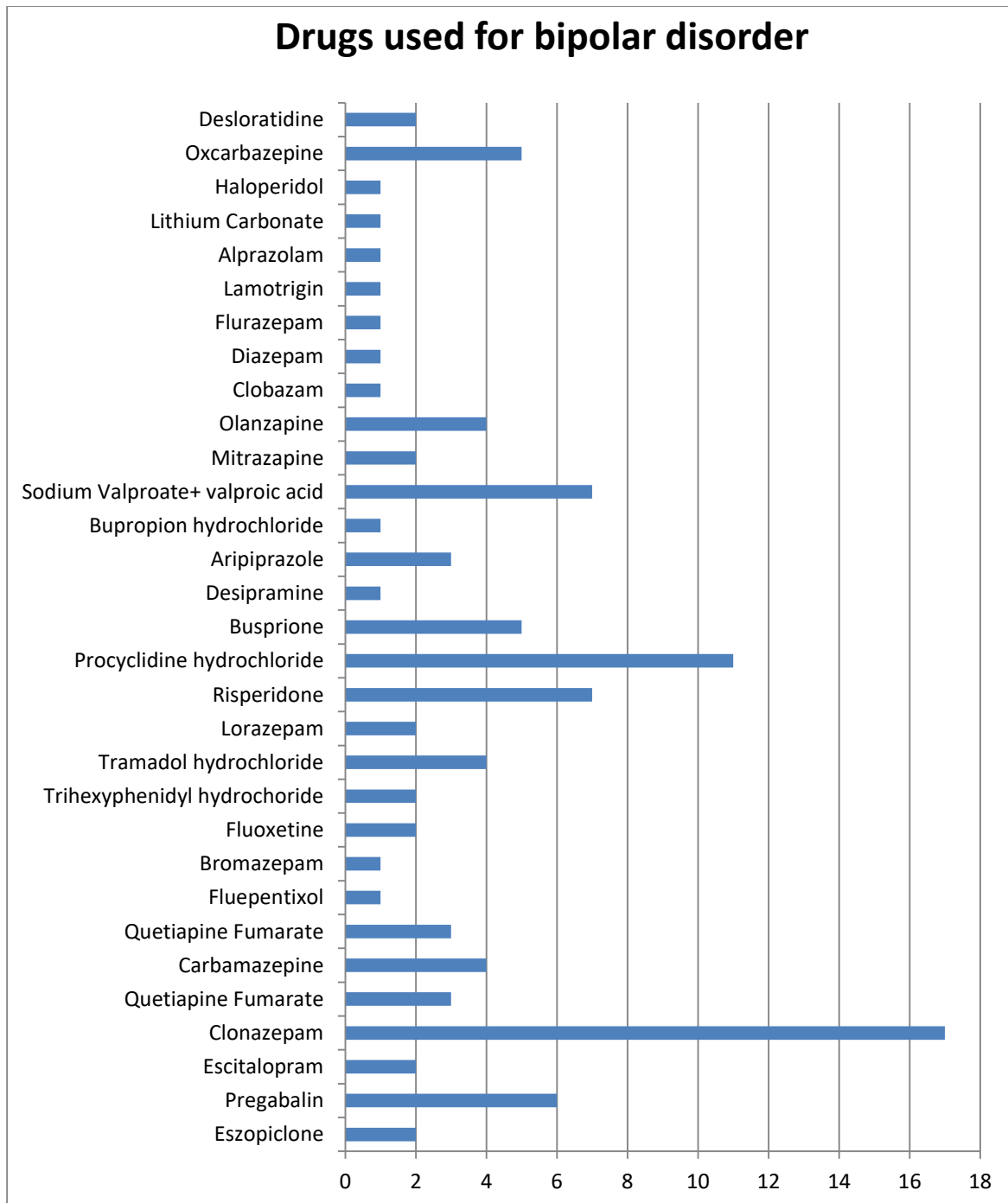


Figure 1.11: The using range of administered drugs by the studied patients

This graph is shown the mostly prescribed medicines by the Bangladeshi doctors to the addicted patient who are suffering from bipolar disorder. Here mentioned the name of 30 drugs that are mostly prescribed. Among those drugs Clonazepam, Procyclidine, Oxcarbazepine, Risperidone,

Pregabalin, Sodium valproate are the mostly prescribed drugs to the drug addicted-bipolar disorder patient.

Chapter-5

Conclusion



Conclusion:

“A retrospective survey analysis on Drug Abuse in Bipolar Disorder on Bangladeshi population”

Bipolar disorder is a mental illness that the sufferer having at least one manic or approximately manic. In our study we find that Methamphetamine is most abusive drug compared to other drugs like Cannabis and benzodiazepine with the age ranges between 15-35 years are found more vulnerable.

Chapter-6

References



1. Bender, R. E., & Alloy, L. B. (2011). Life stress and kindling in bipolar disorder: review of the evidence and integration with emerging biopsychosocial theories. *Clinical psychology review*, 31(3), 383-398.
2. Phillips, M. L., & Kupfer, D. J. (2013). Bipolar disorder diagnosis: challenges and future directions. *The Lancet*, 381(9878), 1663-1671.
3. Leibenluft, E. (2011). Severe mood dysregulation, irritability, and the diagnostic boundaries of bipolar disorder in youths. *American Journal of Psychiatry*, 168(2), 129-142.
4. Craddock, N., & Sklar, P. (2013). Genetics of bipolar disorder. *The Lancet*, 381(9878), 1654-1662.
5. Green, E. K., Grozeva, D., Jones, I., Jones, L., Kirov, G., Caesar, S., ...& Hamshere, M. L. (2010). The bipolar disorder risk allele at CACNA1C also confers risk of recurrent major depression and of schizophrenia. *Molecular psychiatry*, 15(10), 1016-1022.
6. Post, R. M., Leverich, G. S., Kupka, R. W., Keck Jr, P. E., McElroy, S. L., Altshuler, L. L., ... & Suppes, T. (2010). Early-onset bipolar disorder and treatment delay are risk factors for poor outcome in adulthood. *The Journal of clinical psychiatry*, 71(7), 864-872.
7. Kempton, M. J., Salvador, Z., Munafò, M. R., Geddes, J. R., Simmons, A., Frangou, S., & Williams, S. C. (2011). Structural neuroimaging studies in major depressive disorder: meta-analysis and comparison with bipolar disorder. *Archives of general psychiatry*, 68(7), 675-690.
8. Grande, I., Berk, M., Birmaher, B., & Vieta, E. (2016). Bipolar disorder. *The Lancet*, 387(10027), 1561-1572.
9. Berk, M., Kapczinski, F., Andreazza, A. C., Dean, O. M., Giorlando, F., Maes, M., ...& Magalhães, P. V. S. (2011). Pathways underlying neuroprogression in bipolar disorder: focus on inflammation, oxidative stress and neurotrophic factors. *Neuroscience & behavioral reviews*, 35(3), 804-817.
10. Sullivan, P. F., Daly, M. J., & O'Donovan, M. (2012). Genetic architectures of psychiatric disorders: the emerging picture and its implications. *Nature reviews. Genetics*, 13(8), 537.
11. Nestler, E. J., & Hyman, S. E. (2010). Animal models of neuropsychiatric disorders. *Nature neuroscience*, 13(10), 1161-1169.
12. Schmitt, A., Malchow, B., Hasan, A., & Falkai, P. (2014). The impact of environmental factors in severe psychiatric disorders. *Frontiers in neuroscience*, 8.
13. Grande, I., Fries, G. R., Kunz, M., & Kapczinski, F. (2010). The role of BDNF as a mediator of neuroplasticity in bipolar disorder. *Psychiatry investigation*, 7(4), 243-250.
14. Chiu, C. T., Wang, Z., Hunsberger, J. G., & Chuang, D. M. (2013). Therapeutic potential of mood stabilizers lithium and valproic acid: beyond bipolar disorder. *Pharmacological reviews*, 65(1), 105-142.
15. Geddes, J. R., & Miklowitz, D. J. (2013). Treatment of bipolar disorder. *The Lancet*, 381(9878), 1672-1682.

16. Grunze, H., Vieta, E., Goodwin, G. M., Bowden, C., Licht, R. W., Azorin, J. M., ... & Members of the WFSBP Task Force on Bipolar Affective Disorders Working on this topic. (2017). The World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Biological Treatment of Bipolar Disorders: Acute and long-term treatment of mixed states in bipolar disorder. *The World Journal of Biological Psychiatry*, 1-57.
17. Grunze, H., Vieta, E., Goodwin, G. M., Bowden, C., Licht, R. W., Möller, H. J., ... & WFSBP Task Force on Treatment Guidelines for Bipolar Disorders*. (2013). The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of bipolar disorders: update 2012 on the long-term treatment of bipolar disorder. *The World Journal of Biological Psychiatry*, 14(3), 154-219.
18. Grunze, H., Vieta, E., Goodwin, G. M., Bowden, C., Licht, R. W., Möller, H. J., ... & WFSBP Task Force On Treatment Guidelines For Bipolar Disorders. (2010). The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of bipolar disorders: update 2010 on the treatment of acute bipolar depression. *The World Journal of Biological Psychiatry*, 11(2), 81-109.
19. National Collaborating Centre for Mental Health (UK). (2006). Bipolar disorder: The management of bipolar disorder in adults, children and adolescents, in primary and secondary care. British Psychological Society.
20. Goldstein, B. I., Kemp, D. E., Soczynska, J. K., & McIntyre, R. S. (2009). Inflammation and the phenomenology, pathophysiology, comorbidity, and treatment of bipolar disorder: a systematic review of the literature. *The Journal of clinical psychiatry*, 70(8), 1078-1090.
21. Kowatch, R. A., Fristad, M., Birmaher, B., Wagner, K. D., Findling, R. L., & Hellander, M. (2005). Treatment guidelines for children and adolescents with bipolar disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, 44(3), 213-235.
22. Krishnan, K. R. R. (2005). Psychiatric and medical comorbidities of bipolar disorder. *Psychosomatic medicine*, 67(1), 1-8.
23. Weiss, R. D., Griffin, M. L., Kolodziej, M. E., Greenfield, S. F., Najavits, L. M., Daley, D. C., ...& Hennen, J. A. (2007). A randomized trial of integrated group therapy versus group drug counseling for patients with bipolar disorder and substance dependence. *American Journal of Psychiatry*, 164(1), 100-107.
24. Merikangas, K. R., Akiskal, H. S., Angst, J., Greenberg, P. E., Hirschfeld, R. M., Petukhova, M., & Kessler, R. C. (2007). Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Archives of general psychiatry*, 64(5), 543-552.
25. Perugi, G., Vannucchi, G., Bedani, F., & Favaretto, E. (2017). Use of Stimulants in Bipolar Disorder. *Current psychiatry reports*, 19(1), 7.
26. Cheniaux, E., Silva, R. D. A. D., Santana, C. M., & Filgueiras, A. (2017). Changes in energy and motor activity: core symptoms of bipolar mania and depression?. *Revista Brasileira de Psiquiatria*, (AHEAD).
27. Thomas, P., He, F., Mazumdar, S., Wood, J., Bhatia, T., Gur, R. C., ...& Deshpande, S. N. (2017). Joint analysis of cognitive and circadian variation in Schizophrenia and Bipolar I Disorder. *Asian Journal of Psychiatry*.
28. Perich, T., Ussher, J., & Parton, C. (2017). "Is it menopause or bipolar?": a qualitative study of the experience of menopause for women with bipolar disorder. *BMC women's health*, 17(1), 110.

29. Forsberg, L., Adler, M., RömerEk, I., Ljungdahl, M., Navér, L., Gustafsson, L. L., ...& Wide, K. (2017). Maternal mood disorders and lithium exposure in utero were not associated with poor cognitive development during childhood. *Acta Paediatrica*.
30. O'Rourke, N., Heisel, M. J., Canham, S. L., Sixsmith, A., & BADAS Study Team. (2017). Predictors of suicide ideation among older adults with bipolar disorder. *PLoS one*, 12(11), e0187632.
31. Schouws, S. N., Stek, M. L., Comijs, H. C., Dols, A., & Beekman, A. T. (2012). Cognitive decline in elderly bipolar disorder patients: a follow-up study. *Bipolar disorders*, 14(7), 749-755.
32. Iversen, T. S. J., Steen, N. E., Dieset, I., Hope, S., Mørch, R., Gardsjord, E. S., ... & Jönsson, E. G. (2017). Side effect burden of antipsychotic drugs in real life—Impact of gender and polypharmacy. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*.
33. Zhang, B., Shen, C., Ma, G., Fan, H., Wang, J., Zhu, Q., & Wang, W. (2017). Hypnotic susceptibility and affective states in bipolar I and II disorders. *BMC psychiatry*, 17(1), 362.
34. Leclerc, E., Mansur, R. B., Grassi-Oliveira, R., Cordeiro, Q., Kapczinski, F., McIntyre, R. S., & Brietzke, E. (2017). The differential association between history of childhood sexual abuse and body mass index in early and late stages of bipolar disorder. *Journal of affective disorders*, 227, 214-218.
35. Kasahara, T., & Kato, T. (2017). What can mitochondrial DNA analysis tell us about mood disorders?. *Biological psychiatry*.
36. Zalsman, G., Brent, D. A., & Weersing, V. R. (2006). Depressive disorders in childhood and adolescence: an overview. *Child and Adolescent Psychiatric Clinics*, 15(4), 827-841.
37. Keskin, N., Tamam, L., & Ozpoyraz, N. (2016). Assessment of sleep quality in bipolar euthymic patients. *European Neuropsychopharmacology*, 26, S424-S425.
38. Gallur, L., Powell, A., & Flynn, P. (2017). Recommencing lithium in Older Adults with Bipolar I Disorder. *Australasian Psychiatry*, 1039856217738374.
39. Talarowska, M., Bobińska, K., Zajączkowska, M., Su, K. P., Maes, M., & Gałecki, P. (2014). Impact of oxidative/nitrosative stress and inflammation on cognitive functions in patients with recurrent depressive disorders. *Medical science monitor: international medical journal of experimental and clinical research*, 20, 110.
40. Luo, S. X. (2017). Substance use disorders (SUDs) tend to co-occur with attention-deficit/hyperactivity disorder (ADHD)(Kessler et al. 2006; Mariani and Levin 2007; van Emmerik-van Oortmerssen et al. 2012; Wilens 2004; Wilens et al. 1998). The use of psychoactive substances can also be directly implicated in a variety of types of executive dysfunction that may or not be part of ADHD. These dysfunctions can include cardinal symptoms. *Co-occurring Mental Illness and Substance Use Disorders: A Guide to Diagnosis and Treatment*, 93.
41. Mishra, A., Krishna, G. S., Alla, S., Kurian, T. D., Kurian, J., Ramesh, M., & Kishor, M. (2017). Impact of Pharmacist–Psychiatrist Collaborative Patient Education on Medication Adherence and Quality of Life (QOL) of Bipolar Affective Disorder (BPAD) Patients. *Frontiers in pharmacology*, 8, 722.
42. Amini, P., Najafi-Vosough, R., Ghaleiha, A., & Mahjub, H. (2017). Evaluation of Bipolar Disorder in Several Relapses over Time Using Generalized Estimating Equations. *Iranian journal of psychiatry*, 12(3), 182.

43. Hamstra, D. A., de Kloet, E. R., de Rover, M., & Van der Does, W. (2017). Oral contraceptives positively affect mood in healthy PMS-free women: A longitudinal study. *Journal of Psychosomatic Research*, 103, 119-126.
44. McArthur, B. A., Cherry, K. M., Braimoh, G., & Lumley, M. N. (2017). An Exploration of Positive Parenting in Relation to Psychopathology for Youth with a Diagnosis of Bipolar Spectrum Disorder. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, 26(3), 224.
45. Torres, I., Sole, B., Corrales, M., Jiménez, E., Rotger, S., Serra-Pla, J. F., ... & Gómez, N. (2017). Are patients with bipolar disorder and comorbid attention-deficit hyperactivity disorder more neurocognitively impaired?. *Bipolar disorders*.
46. Torres, I., Garriga, M., Sole, B., Bonnín, C. M., Corrales, M., Jiménez, E., ... & Martínez-Aran, A. (2017). Functional impairment in adult bipolar disorder with ADHD. *Journal of Affective Disorders*, 227, 117-125.
47. Bhalla, I. P., Stefanovics, E. A., & Rosenheck, R. A. (2017). Clinical Epidemiology of Single Versus Multiple Substance Use Disorders: Polysubstance Use Disorder. *Medical care*, 55, S24-S32.
48. Azorin, J. M., Perret, L. C., Fakra, E., Tassy, S., Simon, N., Adida, M., & Belzeaux, R. (2017). Alcohol use and bipolar disorders: Risk factors associated with their co-occurrence and sequence of onsets. *Drug & Alcohol Dependence*, 179, 205-212.
49. Williams, S. C., Davey-Rothwell, M. A., Tobin, K. E., & Latkin, C. (2017). People Who Inject Drugs and Have Mood Disorders—A Brief Assessment of Health Risk Behaviors. *Substance Use & Misuse*, 1-10.
50. Messer, T., Lammers, G., Müller-Siecheneder, F., Schmidt, R. F., & Latifi, S. (2017). Substance abuse in patients with bipolar disorder: A systematic review and meta-analysis. *Psychiatry research*, 253, 338-350.
51. Maksimovskiy, A. L. (2017). Neural and cognitive biomarkers of binge and heavy drinking (Doctoral dissertation).
52. Olfson, M., Mojtabai, R., Merikangas, K. R., Compton, W. M., Wang, S., Grant, B. F., & Blanco, C. (2017). Reexamining associations between mania, depression, anxiety and substance use disorders: results from a prospective national cohort. *Molecular psychiatry*, 22(2), 235-241.
53. Lippard, E. T., Mazure, C. M., Johnston, J. A., Spencer, L., Weathers, J., Pittman, B., ... & Blumberg, H. P. (2017). Brain circuitry associated with the development of substance use in bipolar disorder and preliminary evidence for sexual dimorphism in adolescents. *Journal of neuroscience research*, 95(1-2), 777-791.
54. Grunze, H., Vieta, E., Goodwin, G. M., Bowden, C., Licht, R. W., Azorin, J. M., ... & Members of the WFSBP Task Force on Bipolar Affective Disorders Working on this topic. (2017). The World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Biological Treatment of Bipolar Disorders: Acute and long-term treatment of mixed states in bipolar disorder. *The World Journal of Biological Psychiatry*, 1-57.