Original Article

“Relapse Rate Of Bipolar Disorder”

Dr. NAZAR ALI[1] , Dr. Javed Ali[2] , Dr. Hazrat Ali[3] , PROF. DR. GHULAM RASOOL[4] , Dr. Mir Usman[5]

[1]MD PSYCHIATRY DEPARTMENT OF PSYCHIATRY DEPARTMENT, BALOCHISTAN INSTITUTE OF PSYCHIATRY AND BEHAVIORAL SCIENCES QUETTA
[2]DEPARTMENT OF PSYCHIATRY DEPARTMENT, BALOCHISTAN INSTITUTE OF PSYCHIATRY AND BEHAVIORAL SCIENCES QUETTA
[3]DEPARTMENT OF PSYCHIATRY DEPARTMENT, BALOCHISTAN INSTITUTE OF PSYCHIATRY AND BEHAVIORAL SCIENCES QUETTA
[4]MBBS, FCPS DEPARTMENT OF PSYCHIATRY DEPARTMENT, BALOCHISTAN INSTITUTE OF PSYCHIATRY AND BEHAVIORAL SCIENCES QUETTA
[5]DEPARTMENT OF PSYCHIATRY DEPARTMENT, BALOCHISTAN INSTITUTE OF PSYCHIATRY AND BEHAVIORAL SCIENCES QUETTA
DOI: 10.47750/pnr.2022.13.S08.473

Abstract

Recurrent periods of mania, hypomania, mixed moods, and depression characterize bipolar disorder, which is a chronic psychiatric illness. The prevalence of bipolar disorder has been estimated to be between 1% and 2% in various researches. According to the National Comorbidity Survey, the lifetime prevalence is 1.6 percent. Many community survey estimates may not include milder types of bipolar illness, resulting in an underestimating of the true prevalence of the disorder's spectrum. Bipolar illness affects both men and women at similar rates. Over the course of the illness, women appear to be more prone to have mostly depressive rather than manic symptoms. At any age, bipolar disorder (BD) can appear for the first time. According to a survey conducted by the National Depressive and Manic-Depressive Association (NDMDA), 59 % of patients with bipolar disorder first developed symptoms during childhood or adolescence. Bipolar disorder, on the other hand, can appear later in life for the first time. Even with continued treatment, recurrence rates for bipolar disorder remain significant. A 5-year relapse rate of 73 % was discovered in one study, with two-thirds of the patients experiencing numerous relapses. According to other estimates, the relapse rate is around 90%, with approximately half of all relapses happening within two years. The objective of the study is to determine the prevalence of relapse rate of bipolar disorder. The relapse rate in our study was further evaluated on the basis of total numbers of relapse occurred in one year, two years, three years, four years and five years respectively. The result showed that the mean number of relapses in one year was 1.78 ± 1.03 times; in two years was 2.25 ± 0.46 times, in three years 2.64 ± 0.90 times, in four years 3.69 ± 0.837 times and in five years it was found to be 4.24 ± 0.830 times respectively. There was no significant relationship found between relapse rate with gender, marital status, compliance of drug and distribution of age respectively. However, there was significant relationship was found between employment statuses of patients with relapse. (pvalue=0.024*).The healthcare sector faces a big difficulty with bipolar disorder. Misdiagnosis is widespread, and the illness may be more common than previously assumed. Even with continuing treatment, recurrence rates are significant. Bipolar disorder has a wide range of effects on a person's life. Patients with bipolar disorder have a high likelihood of unemployment, and they often struggle in the workplace as well as in social and personal interactions. Bipolar illness patients have a high rate of psychiatric and medical comorbidity, which leads to a higher use of healthcare resources.

KEYWORDS: Bipolar disorder; Depression; Relapse; Recurrence; Treatment.

Introduction:

Bipolar disorder (BD) is a serious mental condition with a high rate of morbidity and mortality in the general population. Suicide ideas (59%) and attempts (56%) are highly related with bipolar disorder, and up to 19% of individuals with bipolar disease die by suicide over their lifetime. This load is linked to relapse of the diseases, and

people with bipolar disorder have a higher family burden of care than patients with other medical illnesses. Relapse in the mental health system refers to becoming unwell again after appearing to have recovered, as well as a worsening of psychiatric patients' condition (Belete, Ali, & Legas, 2020). Relapse of mood episodes, delayed remission, and lingering symptoms are common in psychiatric patients who stop taking medication on their own, against the recommendation of mental health professionals, resulting in hospitalization, increased suicide risk, and/or obstructing psychosocial recovery. Many clinical studies have found that stressful life events always precede bipolar disorder episodes in patients. To avoid recurrence, family-focused psycho-educational psychotherapy appears to be an effective addition to medication. Poor parenting and a history of maltreatment have been linked to a worsening course of bipolar disease. Relapse risk in bipolar people is linked to the psychosocial context of illness, as well as environmental, developmental, and cognitive factors (Cosci & Fava, 2013). 5 As combined with normal psychiatric treatment, adjunctive psychological support reduces recurrence by roughly 40% when compared to standard treatment alone. Relapse has a significant influence on patients' and their families' finances, interpersonal relationships, and quality of life. As a result, understanding the pattern of relapse in low-income nations aids in preventing recurrence and associated health-care costs (Miziou et al., 2015). The severity of relapse differs between researches. According to a follow-up research, 48.5 percent of bipolar illness patients suffered recurrence. Relapses were seen in 34.7 percent of patients with recurrence, and 13.8 percent were having depressed, hypomanic, or mixed episodes. In patients with bipolar illness, the risk of depressive recurrence was 70% higher after a year of successful antidepressant treatment compared to those who stopped taking antidepressants (36 %) (Perlis et al., 2006). A follow-up study found that the recovery rate for bipolar disorder was low, with syndromic recovery occurring in only 48% of cases, symptomatic recovery in only 26% of cases, and functional recovery occurring in only 24% of cases. Relapse is more common in high-risk populations, such as pregnant women, and it can affect up to 71 percent of moms with bipolar illness. Type of diagnosis, earlier onset, more recurrences/year, recent illness, antidepressant use, and anticonvulsant versus lithium use were all revealed to be important factors in this study (Keck Jr et al., 1998). 6 Bipolar I illness is projected to affect 0.6 percent of males and 0.3 percent of women in Ethiopia, according to a community-based study. During the follow-up period, 65.9% of 312 bipolar disorder patients reported a relapse within 2.5 years (47.8 percent manic, 44.3 percent depressive and 7.7 percent mixed episodes, and 31.1 percent had persistent illness). While taking psychotropic medication that was associated with remission, female gender predicted depressed relapse while male gender predicted manic relapse in this study. Despite this greater rate of relapse, there is no data on relapse among bipolar patients in Ethiopian clinical settings (Fekadu et al., 2006; Tran, Tran, & Fisher, 2012). The aim of conducting our study is to determine the prevalence of relapse rate of bipolar disorder. Regrettably, this domain remains not debatable in our society due to bad stigmata on it. This practice eventually puts a huge amount of burden and become a cause of relapse afterwards. The study aims to determine the magnitude of problem in patient with bipolar disease and its subsequent relapse. We believe that once we get the recent results of relapses in patient with bipolar disorder and studying its underlying causes, we may be able to highlight the issues that have remained hidden for the past decades. The results of this study will be compared with the results of international studies that were published in the past and with the integrated approach of assessment and its necessary measurement, we would be able to revise our treatment strategy.

Literature Review:

Bipolar spectrum disorders are a substantial public health issue, with lifetime prevalence estimates ranging from 1.5 to 6.0 percent in the general population of the United States. Bipolar disorder is also linked to a high risk of death, with around 25% of patients attempting suicide and just 11% of patients succeeding. Furthermore, bipolar patients have a high rate of incarceration due to insufficient treatment and service structures. Patients suffering from bipolar depression are still undertreated 31.9 percent of the time after nearly 13 years. (Haro et al., 2006). We have not adequately explored depressive episodes, combination treatment, health services interventions, or unique populations, despite review publications for adults and pediatric patients implying improvement. Although practice guidelines, decision trees, and complex algorithms are well-written, they are not user-friendly (Katz, Goldstein, & Beers, 2001). Psychoeducation, self-help, and psychotherapy (individual, couple, and family) therapies are often used now that more pharmaceutical choices are accessible. The Depression and Bipolar Support Alliance has played a key role in educating

patients, their families, medical professionals, mental health professionals, and the general public about bipolar disorder. 9 The National Alliance of the Mentally Ill (NAMI) has also conducted a poll of family members to learn more about how mental health services are used and valued (Hilty, Brady, & Hales, 1999). Epidemiology Bipolar I disorder typically begins around the age of 18 and bipolar II disorder at the age of 22. The Mood Disorder Questionnaire (MDQ) indicated a prevalence of 3.7 percent in community research. According to the National Comorbidity Study, beginning occurs most commonly between the ages of 18 and 44, with rates greater between the ages of 18 and 34 than between the ages of 35 and 54. In a poll of Depression and Bipolar Support Alliance (DBSA) members, more than half of the patients did not seek therapy for five years, and it took an average of eight years for the accurate diagnosis to be made (J. Angst, Gamma, & Lewinsohn, 2002). Sociodemographic characteristics have not consistently been linked to bipolar disorder. Bipolar I affect both men and women equally, however bipolar II is more common in women. There is no evident link between race/ethnicity, socioeconomic level, and home location (e.g., rural vs. urban). Unmarried people have a higher prevalence of bipolar disorder (Akinhanmi et al., 2018). 10 Direct treatment costs, indirect costs resulting from mortality, and indirect costs resulting from morbidity and lost output are typically included in economic assessments. This is the model for bipolar disorder and other chronic or life-long illnesses. Exorbitant costs and mistreatment result from misdiagnosis. Costs are highly influenced by late presentation, insufficient diagnosis, and undertreatment (Parker, McCraw, Hadzi-Pavlovic, & Fletcher, 2013).

ETIOLOGY AND PATHOPHYSIOLOGY

There is no single concept for bipolar disease that integrates genetic, biochemical, pharmacological, anatomical, and sleeps data. Transmitters (catecholamines, serotonin, gamma aminobutyric acid (GABA), glutamate, and others), hormones (brain-derived neurotrophic factor, thyroid, and others), and steroids (alone and in combination) are all being studied biochemically. Imaging tests, which are becoming more common in medicine, may provide insight (Northoff, Wiebking, Feinberg, & Panksepp, 2011). Affective illnesses are heritable, according to epidemiological research, notably studies of concordance in identical and fraternal twins. Depending on the diagnostic criteria utilized and the heterogeneity of the probands, the morbid risk for family members of bipolar probands ranges from 2.9 to 14.5 percent for bipolar disorder and 4.2 to 24.3 percent for unipolar illness. It's unclear whether 11 bipolar I, bipolar II, hypomania, cyclothymia, and unipolar depression are genetically connected or separate disorders. It's still debatable whether mood disturbance (phenotype) is the greatest predictor of a hereditary cause. Counseling can help patients and their families deal with their worries (Shih, Belmonte, & Zandi, 2004). Biochemical and pharmacologic investigations led to the catecholamine hypothesis to explain bipolar disorder, particularly mania, assuming that mania is caused by an excess of catecholamines whereas depression is caused by depletion. Norepinephrine has been related to depression due to anomalies in the hormone, as well as its manipulation by tricyclic antidepressants (TCAs). Because the dopamine precursor L-dopa, amphetamines, and TCAs frequently cause hypomania in bipolar patients, dopamine has been linked. Severe mania can be treated with antipsychotic drugs that preferentially inhibit dopamine receptors (e.g., pimozide) (Swerdlow & Koob, 1987). Several serotonin ideas have been offered, either alone or in conjunction with other systems. According to the "permissive hypothesis" of serotonin activity, low serotonergic function causes both manic and depressed states by preventing other neurotransmitters from dampening (mainly norepinephrine and dopamine). Certain people believe this explains why some bipolar patients, especially those 12 with uncommon bouts of mania that go away, do better on antidepressants (Riedlinger & Riedlinger, 1994). To learn more about bipolar disorder, researchers are conducting a variety of neuroanatomical and neuroimaging studies. Bipolar disorder is most commonly associated with lesions in the frontal and temporal lobes. Though discrepancies in the posterior regions of the brain may be rectified, left-sided lesions are related with sadness and right-sided lesions with mania (e.g., the association of depression with right parietooccipital lesions) (McCrea, 2008). Computed tomography (CT) scans have repeatedly revealed no abnormalities, however ventricular enlargement has been suggested. Although the therapeutic significance of the findings is unknown, magnetic resonance imaging (MRI) studies reveal an increase in white matter intensity associated with bipolar illness and correlated with age. Most functional imaging investigations (single-photon emission computer tomography [SPECT] and positron emission tomography [PET]) have found prefrontal and anterior paralimbic hypoactivity in bipolar depression patients, while

exploratory studies of manic patients have produced mixed results (Tighe et al., 2012). There are two other prominent bipolar disorder biochemistry models. Electrophysiological kindling and behavioral sensitization, according to Post and colleagues, are at the root of bipolar illness, notably the increased frequency of 13 episodes over time. The following are some of the parallels between this model and bipolar disorder: Early episodes requiring precipitants while later episodes do not; and repeated episodes of one phase leading to the emergence of the other; predisposing effects of both genetic factors and early environmental stress; threshold effects (mild alterations eventually producing full-blown episodes); early episodes requiring precipitants while later episodes do not; and repeated episodes of one phase leading to the emergence of the other (Post, Weiss, Leverich, Smith, & Zhang, 2001). Desynchronization of the circadian rhythm has also been linked to bipolar disorder. Animal studies show that if two rhythms become desynchronized, they can cause recurrent physiological problems (i.e., if one becomes free-running in and out of phase with the other). It's unknown whether or if genetics play a role in the course (e.g., rapid cycling), circadian and seasonal rhythms, and the ability to kindle and sensitize (Carr et al., 2018). Even in euthymic patients, cognitive processing is often impeded in bipolar patients. There have been deficiencies in executive function, visulospatial, memory, linguistic fluency, and attention. This could be a main symptom of bipolar illness, or it could be the result of other disturbances (e.g., sleeplessness) or concomitant conditions (e.g., substance use). In measuring drug side effects, 14 transitioning from inpatient to outpatient care, and using vocational rehabilitation to prepare for job, cognitive testing is neglected (Tsitsipa & Fountoulakis, 2015). DIAGNOSIS Bipolar I disorder, bipolar II disorder, cyclothymic disorder, and bipolar disorder not otherwise specified are all included in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders Text Revision (DSM-IV-TR). Mania, hypomania, depressive, and mixed episodes are the four types of episodes. Patients with bipolar I disorder have had at least one episode of mania by definition. Bipolar II patients have experienced depressed and hypomanic episodes. Although many therapists use the phrase to describe mood fluctuations day to day, rapid cycling formally refers to four or more episodes per year. Secondary mania is defined as mania that occurs as a result of medicine, chemicals, or medical disease and is classified independently (Phillips & Kupfer, 2013). More systematic sampling and more sophisticated detection of people with 1 to 2 symptoms (alone) or 4 to 5 symptoms lasting 2 to 3 days are typically classified as bipolar not otherwise specified, which explains the dramatic growth in epidemiological studies on the "bipolar spectrum." This is a critical judgment because many individuals have previously been diagnosed with depression and 15 have had negative reactions to traditional antidepressants. (McCormick, Murray, & McNew, 2015). Bipolar disorder has a large and complicated differential diagnosis. To begin with, patients' symptoms may resemble those of other mood and psychotic diseases, such as severe depression, schizoaffective disorder, and schizophrenia. Even when individuals appear with severe psychotic symptoms, a positive family history of mood illness is predictive of a mood disorder (Benabarre et al., 2001). Second, bipolar disorder symptoms of recklessness, impulsivity, truancy, and other antisocial behavior are not distinct from those of substance abuse, personality disorders (borderline, antisocial, and others), and attention deficit hyperactivity disorders. Third, while diagnosing bipolar disorder, the relationship between affective disease and personality must be taken into account (Asherson et al., 2014). Bipolar disorder should always be evaluated in the differential diagnosis of depressed individuals, since 3.9 percent of patients converted to bipolar I disorder and 8.6 percent to bipolar II disorder after 2 to 11 years of follow-up. Acute onset of depression, the severity of the depressive episode, and psychosis were all potential predictors of bipolar I disorder, while mood liability, higher rates of substance abuse, disruption of psychosocial functioning, and racing thoughts were all potential predictors of bipolar II disorder (Lobban et al., 2017).

CHALLENGES IN BIPOLAR DISORDER

Poorly managed mood episodes, incomplete remission with cognitive impairment, social dysfunction, and impaired quality of life are all issues that psychiatrists and patients in the United States face. Patients' issues extend beyond the symptoms addressed by available pharmacologic and psychosocial treatments, and many of them reflect the lived negative experience of low self-esteem, impaired sense of identity, isolation, and social stigma, all of which can be exacerbated by insufficient mental health care. (Nestsiarovich et al., 2017). Many of these issues have not been extensively examined since research goals are generally based on disease burden, health expenses, feasibility and

originality of method, donor and advocacy group interests, and expert judgments, rather than patients' viewpoints and concerns. Many writers emphasize the disconnect between research goals and the actual demands indicated by patients, and this bias has been identified as a fundamental flaw in past studies. Stakeholder engagement in research is now widely acknowledged, and substantial study has been done on its practical application, methodology, and evaluation (Rudan et al., 2008). Patients are increasingly being included in research agendas on a legal basis in industrialized nations, transforming them from "passive beneficiaries" to active participants in the planning, design, and evaluation of research, as well as the distribution of its findings. This strategy is based on three primary justifications: I Patients' and their caregivers' unique experiential knowledge can improve the quality and practical 34 relevance of conducted research; (ii) patients' and taxpayers' shared involvement as consumers, taxpayers, voters, and citizens increases trust in research findings and decision-making legitimacy; and (iii) mutual learning between all stakeholders promotes a shared and more objective view of disease phenomena (Abma & Broerse, 2010; Raeymaekers, Crowe, Cowan, Broerse, & Hertz- Pannier, 2016). In Europe, North America, and Australia, new projects have been developed that emphasise multi-stakeholder engagement in research, with mental health coming in second behind oncology (Banfield, Barney, Griffiths, & Christensen, 2014). The Patient-Centered Outcomes Research Institute (PCORI), the Depression and Bipolar Support Alliance (DBSA), the Clinical Trials Transformation Initiative, the FDA's Center for Devices and Radiological Health's Patient Engagement Advisory Committee, and the American Institutes for Research's Center for Patient & Consumer Engagement are among the organizations working in the United States (Stewart, Caird, Oliver, & Oliver, 2011). The Priority Setting Partnership (PSP) methodology of the James Lind Alliance (JLA) in the United Kingdom provides the most comprehensive assessment of the concerns of patients with BD. The study focused on BD research goals relating to etiology, diagnosis, treatment, support, and prognosis in 3283 patients, carers, and health care professionals who answered 14 492 questions in surveys about these 35 topics. BD etiology, tailored treatment, and a combination of self-management techniques, counseling, and medication were among the "top 10" priorities for BD research that emerged (Robinson et al., 2006).

RELAPSE

Regardless of what their prior episode entailed, people with bipolar disorder might relapse with manic, mixed, or depressed episodes. Differential response to therapies and other factors linked with the condition complicate the risk of relapse. It's especially important to avoid the onset of rapid cycling symptoms if you want to have a positive outcome (Perlis et al., 2006). According to data of moderate quality, the likelihood of a future mood episode after a first mood episode is roughly 44% in the first year, then drops to around 20% in the second and third years. Adolescents had persistent recurrence rates of around 20% over three years. After a first mood episode, the typical interval between future mood episodes is roughly 1.5 years. Persons with bipolar I disorder take longer than people with bipolar II illness, adolescents take longer than adults, people tested in a euthymic phase take longer than people tested in a mood phase, and people with persisting subclinical symptoms take longer. Children and adolescents with bipolar disorder were more likely than children and adolescents with other psychiatric diseases to be readmitted to a psychiatric hospital (Molenaar et al., 2019). 37 Evidence of moderate to low quality suggests that following a first episode of depression, there is a minor effect of a higher likelihood of any subsequent mood episode than after a first episode of mania or mixed symptoms. People with bipolar II disorder had a greater probability of a depressive following mood episode than those with bipolar I disease. The polarity of the index episode, on the other hand, was often predictive of the polarity of the second episode (Franzen & Buysse, 2008). Relapse rates for those who have had their first episode of mania are around 26% after six months and up to 48% after four years, according to moderate quality research. Lower relapse rates were linked to older age at the initial bout of mania. Relapse rates for patients with a first episode of mania or mixed symptoms range from 35 percent after 12 months to 58 percent after four years, according to moderate to low quality evidence (Rowland & Marwaha, 2018). There is intermediate to low quality evidence for pregnant women, indicating that the median rate of mood episodes during pregnancy is roughly 24%, with the majority of episodes being depressive. Mood relapse rates in postpartum women are around 37%, which is similar to psychotic relapse rates in women with a history of postpartum psychosis, although severe relapses are more common in women

with a history of postpartum psychosis. Those who used preventative 38 drugs throughout pregnancy or after delivery had fewer relapses than women who did not take any during pregnancy (Wesseloo et al., 2016).

Lobban et al. developed an upgraded version of RP to be used alongside other therapies such as medication to see if generalizable deployment was viable utilising routinely available community mental health services (Lobban et al., 2007). Care coordinators (CCs), who are psychiatric nurses, social workers, or occupational therapists who practise case management from community work bases (Community Mental Health Teams or CMHTs) with psychiatrists and clinical psychologists in the UK NHS, provide Enhanced Relapse Prevention 43 (ERP). Many services around the world, but not all, have a comparable structure for providing community follow-up treatment for patients with significant mental illness. The ERP intervention is accompanied by an easy-to-follow guidebook that outlines each of the six sixty-minute sessions and is reviewed by service users (SUs), family, and community coordinators (CCs) (Morgan, Mitchell, & Jablensky, 2005; Mueser, Bond, Drake, & Resnick, 1998).

Research Methodology:

OPERATIONAL DEFINTIONS: - 1. Bipolar Disorder: - It was defined as state of mental illness that brings severe fluctuation in moods from high and low and vice versa as well as changes in sleep, energy, thinking, and behavior. It was evaluated on the basis of diagnostic and statistical manual of mental disorders (DSM-5) bipolar .In this study we have assessed two types of bipolar disorders, type 1 and type 2. 2. Relapse rate: - It was defined as the return of depression or a manic or hypomanic episode after a period of wellness. Depression or manic episode will be judged according the above-mentioned criteria of bipolar disorder. The relapse rate was assessed in patients with history of bipolar disorders previously diagnosed at least 1 year back who are on routine visit to outpatient department.

MATERIAL AND METHOD: Study design: Cross sectional (Descriptive study). 46 Setting: Balochistan institute of psychiatry and behavioral sciences Quetta. Duration of study: The study took six months from 1st July 2021 to 31st December 2021. Sample size: For the objective of the study, sample size has been calculated by using WHO sample size calculator with Confidence level (1-α) is taken as 95%, with desired precision (d) of 8 % and approximate population estimation (frequency of burnout syndrome among medical professionals) of 71 % taken from the parent study (Belete et al., 2020). By putting all the values, the largest sample size calculated was 123. n= Z1-α/2 2 * P (1-P)/d2 where; p= estimated prevalence= 0.71 q= 1-p= 0.29 d= margin of error 0.08 α= probability of type 1 error 0.05 (2-sided) = 1.96 Sampling technique: non-probability consecutive sampling.

SAMPLE SELECTION: - Inclusion Criteria: - 1. All individuals age 18 years- 65 years who were previously admitted at least one year back with bipolar disorders and were treated and discharged home and have been on routine outpatient follow up were included. 2. Either gender. Exclusion Criteria: - 1. Any patient with bipolar disorder however diagnosed in less than 1 year. 2. Any individual with any other psychiatric diagnoses along with bipolar disease. 3. History of any psychosurgery with bipolar disease was excluded. All above mentioned cases were effect modifier, and if included in the sample then would have introduced bias in the study results.

DATA COLLECTION TECHNIQUE: -The study was conducted after the approval from Dean/ Director of Postgraduate Medical Institute, Balochistan institute of psychiatry and behavioral sciences Quetta. All individuals who were admitted previously with diagnosis of bipolar disorder and treated and discharged home safely at least 1 year back were included. Written consent was from patient or guardian before conducting the study. A detailed history was taken for each patient. Proforma was filled for patient ID number, sex and age of all patients with 48 history of bipolar disease. Relapse was documented at least after 1 year of diagnosis of bipolar disorder till 5 years after diagnosis. Later, results were analyzed by senior resident who was part of the team of conducting this study which again was checked by consultant before putting the data onto proforma.

DATA ANALYSIS PROCEDURE: - Data was compiled and analyzed using statistical package for social sciences (SPSS) version 26.0. Mean ± Standard deviation (SD) were calculated for quantitative variables like age, duration of illness, numbers of admission in hospital, total number of relapses at 1 year, 2 years, 3 years, 4 years, and 5 years.

Frequencies with percentages were presented for qualitative variables and categorical variables like marital status (single/married/divorced), compliance of drugs (yes/no), relapse (yes/no) and employment status (employed/ unemployed). Effect modifiers were controlled through stratification of age, marital status and compliance of drugs to see the effect of these on outcome variables. By applying P value of ≤0.05 was considered as statistically significant.

Results:

There was total 128 patients of bipolar disorder were enrolled in the study. Of them 95 were males and 33 were females that constitute about 74% and 26% respectively. The mean age of patients was 43.87 ± 11.39 years. Moreover, the mean duration of patient 's illness was found to be 4.53 ± 2.79 years and mean number of previous admissions in hospital was found to be 2.91 ± 0.972 times respectively. In our study, patients were assessed on the basis of their marital status. Out of 128 individuals, 74 were found married while 33 were single and 21 were found divorced respectively that comprises of 58%, 26% and 16% respectively. Similarly, evaluation of patients was also done on the bass of compliance of drug intake. Out of 128 patients, 71 were found to have good compliance while 57 had poor dose compliance that constitutes about 56% and 44% respectively . In our study, the frequency of relapse rate in patients with bipolar disorder was found to be 36%. That means out of 128 subjects, 46 were found to have relapse in our study (Figure-8). The relapse rate in our study was further evaluated on the basis of total numbers of relapse occurred in one year, two years, three years, four years and five years 51 respectively. The result showed that the mean number of relapse in one year was 1.78 ± 1.03 times; in two years was 2.25 ± 0.46 times, in three years 2.64 ± 0.90 times, in four years 3.69 ± 0.837 times and in five years it was found to be 4.24 ± 0.830 times respectively . Likewise, subjects were also assessed on the basis of their employment status. Out of 128 subjects, 41 were employed while 87 were unemployed constituting about 32% and 68% respectively . Distribution of age was also analyzed in our study that was categorized into 18-35 age group, 36-50 age group and 51-65 years old age groups respectively. Out of 128 total patients, 38 were in between age group 18-35 years old, 53 were in between age group 36-50 years old and 37 were in between age groups 51-65 years old. That comprises of 30%, 41% and 29% correspondingly . Furthermore, in our study; relation between relapse was evaluated with gender. Out of 46 patients, in which relapse was occurred; 32 were males and 14 were females. However, there was no significant relationship was found between relapse and gender statistically . Likewise, relationship between relapse in patients with bipolar disorder was assessed with marital status of patients. Out of 46 patients who had relapse, 13 were found single, 25 were found married and only 8 were found divorced. 52 However, statistically; no significant relationship was found between them with p-value >0.05 respectively . Similarly, there was no significant relation was found between relapse with compliance of drug and distribution of age respectively . In our study, there was significant relationship was found between employment statuses of patients with relapse. Out of 46 patients, who had relapse; only 9 were employed whereas 37 were unemployed (p-value=0.024*)

Discussion:

The results of this study revealed that recurrence was associated with various predictors including gender, marital status, distribution of age, compliance of drug and employment status of patients. In our study males with bipolar disorder more likely to developed relapse compared to female. This could be because due to the fact that more males were enrolled in the study compared to females. In terms of distribution of gender with respect to proportion, more females (42%) were affected with relapse compared to males (34%) respectively. Almost similar results were shown in study conducted by Lesly who demonstrated that females patients with bipolar disorder was affected more compared to males patients with this disorder respectively (L. M. Arnold, 2003). In this study, assessment of patients who had relapse was done with marital status. Results showed that married individuals were more affected with relapse followed by single and then divorced. However there was no significant relationship was found between them. Similar findings were demonstrated in study conducted by Omran et al who showed that relapse was seen in mostly married people compared to those who were single or divorced (Davarinejad et al., 2021). 70 Ghoreishizadeh et al. looked at risk factors for relapse of bipolar I illness based only on the frequency of observable circumstances, however recurrence was more common in divorced or widowed people than married or single people (QureshiZadeh, Ranjbar,

& Pezeshki, 2009). Due to the lengthy treatment process, patient care is difficult, resulting in despair, erosion, occurrence, or worsening of psychosomatic disorders in other family members, particularly the patient's parents and spouse (Pickett-Schenk, Cook, & Laris, 2000). Given the difficulty of caring for mentally ill patients, the loss of this supportive focus (divorce or death of a spouse) may raise the likelihood of recurrence in these individuals. When it comes to bipolar disorder, treatment adherence is crucial. According to numerous studies, more than 60% of patients do not adhere to treatment. Relapse is more likely if you don't stick to your treatment plan and stop taking your mood stabilisers (Gaudiano, Weinstock, & Miller, 2008). The findings of this study revealed that patients who stopped taking their medications had a higher risk of recurrence. However, there was no statistically significant link between them. In our study, employment status was shown to have significant relationship with relapse or recurrence in patients with bipolar disorder. Dickerson et al. (Dickerson et al., 2004) looked at the link between cognitive functioning and employment status in people with bipolar disorder, and found that current employment status was substantially linked to mental hospitalization history. 71 Previous hospitalizations may suggest fewer relapses throughout the illness's course. In our study, the frequency of relapse rate in patients with bipolar disorder was found to be 36%. Distribution of age was also shown to have insignificant relationship with relapse in our study. Though the most common age group affected was patients who fall in 36-50 years old age group. On the other hand, literature showed that younger teenagers have increase tendency to develop relapse compared to old age patients (Sajatovic, 2005).

Conclusion:

The healthcare sector faces a big difficulty with bipolar disorder. Misdiagnosis is widespread, and the illness may be more common than previously assumed. Even with continuing treatment, recurrence rates are significant. Bipolar disorder has a wide range of effects on a person's life. It's usual to lose function, and the quality of life suffers as a result. Patients with bipolar disorder have a high likelihood of unemployment, and they often struggle in the workplace as well as in social and personal interactions. Bipolar illness patients have a high rate of psychiatric and medical comorbidity, which leads to a higher use of healthcare resources.

References:

- Abma, T. A., & Broerse, J. E. (2010). Patient participation as dialogue: setting research agendas. Health Expectations, 13(2), 160-173.
- • Akinhanmi, M. O., Biernacka, J. M., Strakowski, S. M., McElroy, S. L., Balls Berry, J. E., Merikangas, K. R., . . . LeBoyer, M. (2018). Racial disparities in bipolar disorder treatment and research: a call to action. Bipolar disorders, 20(6), 506-514.
- • Alper, J., Friedman, K., Graig, L., National Academies of Sciences, E., & Medicine. (2020). Proceedings of a Workshop. Paper presented at the Caring for People with Mental Health and Substance Use Disorders in Primary Care Settings: Proceedings of a Workshop.
- • Angst, F., Stassen, H. H., Clayton, P. J., & Angst, J. (2002). Mortality of patients with mood disorders: follow-up over 34–38 years. Journal of affective disorders, 68(2-3), 167-181.
- • Angst, J., Gamma, A., & Lewinsohn, P. (2002). The evolving epidemiology of bipolar disorder. World psychiatry, 1(3), 146.
- • Arnold, B. F., Ercumen, A., Benjamin-Chung, J., & Colford Jr, J. M. (2016). Brief report: negative controls to detect selection bias and measurement bias in epidemiologic studies. Epidemiology (Cambridge, Mass.), 27(5), 637.
- • Arnold, L. M. (2003). Gender differences in bipolar disorder. Psychiatric Clinics, 26(3), 595-620.
- • Asherson, P., Young, A. H., Eich-Höchli, D., Moran, P., Porsdal, V., & Deberdt, W. (2014). Differential diagnosis, comorbidity, and treatment of attention-deficit/hyperactivity disorder in relation to bipolar disorder or borderline personality disorder in adults. Current medical research and opinion, 30(8), 1657-1672.
- • Baer, L. (1996). Behavior therapy: endogenous serotonin therapy? The Journal of clinical psychiatry, 57, 33-35. 75
- • Banfield, M. A., Barney, L. J., Griffiths, K. M., & Christensen, H. M. (2014). Australian mental health consumers' priorities for research: qualitative findings from the SCOPE for Research project. Health Expectations, 17(3), 365-375.
- • Belete, H., Ali, T., & Legas, G. (2020). Relapse and Clinical Characteristics of Patients with Bipolar Disorders in Central Ethiopia: A Cross-Sectional Study. Psychiatry journal, 2020
- . • Benabarre, A., Vieta, E., Colom, F., Martinez-Aran, A., Reinares, M., & Gasto, C. (2001). Bipolar disorder, schizoaffective disorder and schizophrenia: epidemiologic, clinical and prognostic differences. European Psychiatry, 16(3), 167-172.
- • Berridge, M. J., Downes, C. P., & Hanley, M. R. (1989). Neural and developmental actions of lithium: a unifying hypothesis. Cell, 59(3), 411- 419.
- • Black, C. J., Thakur, E. R., Houghton, L. A., Quigley, E. M., Moayyedi, P., & Ford, A. C. (2020). Efficacy of psychological therapies for irritable bowel syndrome: systematic review and network meta-analysis. Gut, 69(8), 1441-1451.

- • Bond, K., & Anderson, I. M. (2015). Psychoeducation for relapse prevention in bipolar disorder: a systematic review of efficacy in randomized controlled trials. Bipolar disorders, 17(4), 349-362.
- • Bouton, M. E., Maren, S., & McNally, G. P. (2021). Behavioral and neurobiological mechanisms of Pavlovian and instrumental extinction learning. Physiological reviews, 101(2), 611-681.
- • Bowden, C. L. (2005). A different depression: clinical distinctions between bipolar and unipolar depression. Journal of affective disorders, 84(2-3), 117-125.
- • Carr, O., Saunders, K. E., Bilderbeck, A. C., Tsanas, A., Palmius, N., Geddes, J. R., . . . Goodwin, G. M. (2018). Desynchronization of diurnal rhythms in bipolar disorder and borderline personality disorder. Translational psychiatry, 8(1), 1-9.
- • Coenen, V. A., Panksepp, J., Hurwitz, T. A., Urbach, H., & Mädler, B. (2012). Human medial forebrain bundle (MFB) and anterior thalamic radiation (ATR): imaging of two major subcortical pathways and the dynamic balance of opposite affects in understanding depression. The Journal of neuropsychiatry and clinical neurosciences, 24(2), 223-236.
- • Colizzi, M., Lasalvia, A., & Ruggeri, M. (2020). Prevention and early intervention in youth mental health: is it time for a multidisciplinary and trans-diagnostic model for care? International journal of mental health systems, 14(1), 1-14.
- • Colom, F., Vieta, E., Martinez, A., Jorquera, A., & Gasto, C. (1998). What is the role of psychotherapy in the treatment of bipolar disorder? Psychotherapy and Psychosomatics, 67(1), 3-9.
- • Cosci, F., & Fava, G. A. (2013). Staging of mental disorders: systematic review. Psychotherapy and Psychosomatics, 82(1), 20-34.
- • Davarinejad, O., Mohammadi Majd, T., Golmohammadi, F., Mohamadi, P., Radmehr, F., Nazari, S., & Moradinazar, M. (2021). Factors Influencing the Number of Relapse in Patients with Bipolar I Disorder. Shiraz E-Medical Journal(In Press).
- • Deacon, B. J. (2013). The biomedical model of mental disorder: A critical analysis of its validity, utility, and effects on psychotherapy research. Clinical psychology review, 33(7), 846-861.
- • Dickerson, F. B., Boronow, J. J., Stallings, C. R., Origoni, A. E., Cole, S., & Yolken, R. H. (2004). Association between cognitive functioning and employment status of persons with bipolar disorder. Psychiatric Services, 55(1), 54-58. 77
- • Fekadu, A., Kebede, D., Alem, A., Fekadu, D., Mogga, S., Negash, A., . . . Shibre, T. (2006). Clinical outcome in bipolar disorder in a community- based follow-up study in Butajira, Ethiopia. Acta Psychiatrica Scandinavica, 114(6), 426-434.
- • Fletcher, K., Parker, G., Paterson, A., & Synnott, H. (2013). High-risk behaviour in hypomanic states. Journal of affective disorders, 150(1), 50- 56.
- • Franzen, P. L., & Buysse, D. J. (2008). Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. Dialogues in clinical neuroscience, 10(4), 473.
- • Haro, J. M., Arbabzadeh-Bouchez, S., Brugha, T. S., De Girolamo, G., Guyer, M. E., Jin, R., . . . Vilagut, G. (2006). Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health surveys. International journal of methods in psychiatric research, 15(4), 167-180. 78
- • Hibbeln, J. R., Umhau, J. C., George, D. T., & Salem Jr, N. (1997). Do plasma polyunsaturates predict hostility and depression? World review of nutrition and dietetics, 82, 175-186.
- • Hilty, D. M., Brady, K. T., & Hales, R. E. (1999). A review of bipolar disorder among adults. Psychiatric Services, 50(2), 201-213.
- • Hilty, D. M., Leamon, M. H., Lim, R. F., Kelly, R. H., & Hales, R. E. (2006). A review of bipolar disorder in adults. Psychiatry.
- • Kandel, E. R. (1979). Psychotherapy and the single synapse. New England Journal of Medicine, 301(19), 1028-1037. •
- Kapczinski, F., Vieta, E., Andreazza, A. C., Frey, B. N., Gomes, F. A., Tramontina, J., . . . Post, R. M. (2008). Allostatic load in bipolar disorder: implications for pathophysiology and treatment. Neuroscience & Biobehavioral Reviews, 32(4), 675-692.
- • Katz, L. J., Goldstein, G., & Beers, S. R. (2001). Learning disabilities in older adolescents and adults: Clinical utility of the neuropsychological perspective.
- • Keck Jr, P. E., McElroy, S. L., Strakowski, S. M., West, S. A., Sax, K. W., Hawkins, J. M., . . . Haggard, P. (1998). 12-month outcome of patients with bipolar disorder following hospitalization for a manic or mixed episode. American Journal of Psychiatry, 155(5), 646-652.
- • Lauder, S. D., Berk, M., Castle, D. J., Dodd, S., & Berk, L. (2010). The role of psychotherapy in bipolar disorder. Medical Journal of Australia, 193, S31-S35
- • Malhi, G. S., Gessler, D., & Outhred, T. (2017). The use of lithium for the treatment of bipolar disorder: recommendations from clinical practice guidelines. Journal of affective disorders, 217, 266-280.
- • Mandell, A. J., & Knapp, S. (1979). Asymmetry and mood, emergent properties of serotonin regulation: A proposed mechanism of action of lithium. Archives of general psychiatry, 36(8), 909-916.
- • Manji, H. K. (1992). G proteins: implications for psychiatry. The American journal of psychiatry. •
- McCormick, U., Murray, B., & McNew, B. (2015). Diagnosis and treatment of patients with bipolar disorder: A review for advanced practice nurses. Journal of the American Association of Nurse Practitioners, 27(9), 530-542.
- • McCrea, S. M. (2008). Bipolar disorder and neurophysiologic mechanisms. Neuropsychiatric disease and treatment, 4(6), 1129.
- • McFarlane, W. R. (2016). Family interventions for schizophrenia and the psychoses: A review. Family Process, 55(3), 460-482.
- • McInerney, S. J., & Kennedy, S. H. (2014). Review of evidence for use of antidepressants in bipolar depression. The primary care companion for CNS disorders, 16(5).
- • McInnis, M. G., McMahon, F. J., Chase, G. A., Simpson, S. G., Ross, C. A., & DePaulo Jr, J. R. (1993). Anticipation in bipolar affective disorder. American journal of human genetics, 53(2), 385.

. • Stefanis, C. N., & Stefanis, N. C. (2002). Diagnosis of depressive disorders: A review. Depressive disorders, 1-87.

• Stewart, R. J., Caird, J., Oliver, K., & Oliver, S. (2011). Patients‘ and clinicians‘ research priorities. Health Expectations, 14(4), 439-448.

• Subodh, B., Sharma, N., & Shah, R. (2018). Psychosocial interventions in patients with dual diagnosis. Indian Journal of Psychiatry, 60(Suppl 4), S494.

• Swerdlow, N. R., & Koob, G. F. (1987). Dopamine, schizophrenia, mania, and depression: toward a unified hypothesis of cortico-striatopallidothalamic function. Behavioral and brain sciences, 10(2), 197-208.

• Tighe, S. K., Reading, S. A., Rivkin, P., Caffo, B., Schweizer, B., Pearlson, G., . . . Bassett, S. S. (2012). Total white matter hyperintensity volume in bipolar disorder patients and their healthy relatives. Bipolar disorders, 14(8), 888-893.

• Tiihonen, J., Haukka, J., Henriksson, M., Cannon, M., Kieseppä, T., Laaksonen, I., . . . Lönnqvist, J. (2005). Premorbid intellectual functioning in bipolar disorder and schizophrenia: results from a cohort study of male conscripts. American Journal of Psychiatry, 162(10), 1904-1910.

• Tran, T. D., Tran, T., & Fisher, J. (2012). Validation of three psychometric instruments for screening for perinatal common mental disorders in men in the north of Vietnam. Journal of affective disorders, 136(1-2), 104-109.

• Tsitsipa, E., & Fountoulakis, K. N. (2015). The neurocognitive functioning in bipolar disorder: a systematic review of data. Annals of general psychiatry, 14(1), 1-29. 85

• Vieta, E., Langosch, J. M., Figueira, M. L., Souery, D., BlascoColmenares, E., Medina, E., . . . Bellivier, F. (2013). Clinical management and burden of bipolar disorder: results from a multinational longitudinal study (WAVE-bd). International journal of neuropsychopharmacology, 16(8), 1719-1732.

• Volkmann, C., Bschor, T., & Köhler, S. (2020). Lithium treatment over the lifespan in bipolar disorders. Frontiers in Psychiatry, 11, 377.

• Wehr, T. A., Turner, E. H., Shimada, J. M., Lowe, C. H., Barker, C., & Leibenluft, E. (1998). Treatment of a rapidly cycling bipolar patient by using extended bed rest and darkness to stabilize the timing and duration of sleep. Biological psychiatry, 43(11), 822-828.

• Wesseloo, R., Kamperman, A. M., Munk-Olsen, T., Pop, V. J., Kushner, S. A., & Bergink, V. (2016). Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. American Journal of Psychiatry, 173(2), 117-127.

• Wong, M.-L., & Licinio, J. (2001). Research and treatment approaches to depression. Nature Reviews Neuroscience, 2(5), 343-351.

• Worley, P. F., Baraban, J. M., & Snyder, S. H. (1987). Beyond receptors: Multiple second-messenger systems in brain. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society, 21(3), 217-229.

• Yehuda, R., Hoge, C. W., McFarlane, A. C., Vermetten, E., Lanius, R. A., Nievergelt, C. M., . . . Hyman, S. E. (2015). Post-traumatic stress disorder. Nature Reviews Disease Primers, 1(1), 1-22.

• Zarate, C. A., Tohen, M., Land, M., & Cavanagh, S. (2000). Functional impairment and cognition in bipolar disorder. Psychiatric Quarterly, 71(4), 309-329