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Original Article

Role of Excessive Caffeine in Triggering Bipolar Affective Disorder

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ABSTRACT

Objective: To analyze the impact of excessive caffeine consumption, causing sleep disturbance and consequent triggering of the onset or relapse among patients with bipolar affective disorder.
Study Design: Analytical cross-sectional study.
Place and Duration of study: Armed Forces Institute of Mental Health (AFIMH), Rawalpindi, Pakistan, from Nov 2021 to Apr 2022.
Methodology: A total of 110 patients, aged 20-60 years and diagnosed with bipolar affective disorder, were evaluated for triggering effect on disease after excessive caffeine intake of at least 180mg/day, in the last 2 weeks, along with effect of other triggering factors with or without caffeine. All data was analysed using SPSS.
Results: A total of 69% of patient's disease was triggered due to excessive caffeine alone and combined with factors of stress and non-adherence. Based on scores using Athens insomnia rating scale, 99% of our patients fulfilled the criteria for sleep disturbance.
Conclusion: Excessive caffeine use significantly impairs sleep and thus contribute to onset or relapse of symptoms in patients with bipolar affective disorder.

Keywords: Bipolar disorder, Caffeine, Sleep, Trigger.

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INTRODUCTION

Globally, caffeine is the most consumed stimulant with notable effects being psychomotor activation,[1] cognitive enhancement and physical strength with evidence of positive impact on Alzheimer's disease, Parkinson's disease and recurrent depression.[2] Caffeinated dietary sources include tea, coffee, energy drinks, cocoa and chocolate, making it a mood enhancer which increases alertness by delaying sleep onset.[3] Due to its competitive antagonism on striatal adenosine A1 and A2A receptors, effecting D1 and D2 receptors respectively, by releasing dopamine, glutamate, and acetylcholine, caffeine induces mania or psychosis in predisposed individuals.[4] In Diagnostic and Statistical Manual of Mental Disorders (DSM),[5] caffeine consumption of more than 250 mg/day falls under caffeine intoxication with harmful effects 5 like insomnia, psychomotor agitation, mood elation, rapid speech and periods of inexhaustibility. Doses of more than 300mg are associated with new onset mania, delayed recovery in bipolar patients, mood fluctuation and anxiety symptoms.[1] Excessive use of caffeine in the past decade and rise in mental disorders have been reported in literature.[2] Our study aims to determine the impact of caffeine in triggering bipolar illness. Bipolar affective disorder is a severe, chronic mental illness with relapsing, remitting pattern and episodes of hypomania/mania and depression along with psychosocial impairment, which is linked to contributing factors like disturbed sleep, stressors, non-adherence to treatment, substance use and previous hospitalizations, all of which can impact long-term outcomes.[6] This study aimed to identify the relation between excessive caffeine, sleep disturbance and development or relapse of bipolar disorder. Our study will contribute to awareness about careful monitoring of use of stimulants like caffeine in psychiatric and general clinical settings while also enabling judicious use of sedatives and hypnotics in incorporation of sleep hygiene principles in vulnerable population.

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METHODOLOGY

This analytical cross-sectional study was conducted from November 2021 to April 2022 at Armed Forces Institute of Mental Health (AFIMH), Rawalpindi, Pakistan, after an approval from Ethics Committee of the institute (S.no 0022/21) was granted. A sample size of 110 was calculated with Raosoft calculator, keeping population proportion at 59%

(caffeine users with manic episode),1 population size at approximately 150 and confidence level of 95%. Participants were selected by non-probability purposive sampling among all patients presenting to AFIMH, who consented and were selected as per the inclusion criteria from outpatient and inpatient department after establishing the diagnosis based on International Classification of Diseases (ICD)-10 criteria.

Inclusion Criteria: Patients, both male and female, aged 20-60 years, diagnosed with onset or relapse of bipolar affective disorder, and those who provided consent were included in the study.

Exclusion criteria: Patients with bipolar disorder in remission, organic illnesses, substance dependents (except nicotine and caffeine), all other psychiatric disorders and those who did not consent, were excluded.

Semi-structured questionnaire and Athens insomnia scale were introduced to the selected participants and collected data was divided into two categories, based on the triggering factor, with or without excessive caffeine intake at least >180/day in last 2 weeks. Daily caffeine intake was estimated through a structured self-report questionnaire. Participants were asked to report their regular sources of caffeine consumption, including tea, coffee, carbonated beverages, energy drinks, and chocolate. In the present sample, tea was identified as the predominant source of caffeine intake. Participants were asked to specify the number of cups or servings consumed per day. The approximate caffeine content of commonly consumed beverages was used to estimate the total daily caffeine intake. Based on the reported frequency of consumption, the total caffeine intake per day was calculated and categorized into the following groups: 45–90 mg, 90–135 mg, 135–180 mg, 180–225 mg, 225–270 mg, 270–315 mg, 315–360 mg, 360–400 mg, and >400 mg per day. The data was then analyzed with the help of Statistical Package for Social Sciences (SPSS) version 20.00 where quantitative variables, like age, were presented as Mean±SD, and qualitative variables, like gender, marital status and current Bipolar episode, were measured in frequencies and percentages. For comparative aspects between different categories, chi-square test was used where a *p*-value≤0.05 was considered as significant. Frequencies and percentages for onset, or relapse of bipolar disorder, were examined in relation to gender, caffeine intake, non-adherence to medication and other causative factors alone and combined using cross-tabulation method in descriptive statistics.

RESULTS

Out of 110 enrolled participants, 34(31.00%) patients were in age group 50 and above, followed by 27.00% patients in age group 40 and above, while the lowest percentage (16.40 %) was noted in patients in age group 20 and above.

Table-I: Frequency of Demographic Variables (n=110)

Study Parameter(s)	Values
Mean Age (Years)	2.72 ± 1.08
Age (Years)	
20 – 29	19 (17.80%)
30 – 39	27 (24.50%)
40 – 49	30 (27.30%)
50 - 59	34 (30.90%)
Gender	
Male	82(74.50%)
Female	28(25.50%)
Marital Status	
Single	21(19.10%)
Married	84(76.40%)
Separated/Divorced	3(2.70%)
Widow-Widower	2(1.80%)
Patients presented with type of Bipolar disease	
1st manic episode	13(11.80%)
Relapse of Bipolar affective disorder –Manic episode	77(70.00%)
Relapse of Bipolar affective disorder-Mania with psychosis	15(13.60%)
Mixed Affective state	5(4.50%)
Adherence to medication	
Yes	50(45.50%)
Erratic /Irregular	44(40.00%)
Not Applicable (1st episode mania)	16(14.50%)
Total amount of Caffeine consumed /day	
45-90mg	16(14.50%)
90-135mg	17(15.50%)
135-180mg	12(10.90%)
180-225mg	22(20.00%)
225-270mg	15(13.60%)
270-315mg	8(7.30%)
315-360mg	4(3.60%)
360-400mg	4(3.60%)
more than 400mg	8(7.30%)
Nil	4(3.60%)
Insomnia on Athens insomnia scale	
Insomnia	109(99.10%)
No insomnia	1(0.90%)

As shown in Table-I, 74.50% of our patients were males while 28.00% were females, among which 84 (76.40%) patients were married while 19.00% were unmarried. In our study, 70.00% of patients presented with relapse of mania without psychosis, 13.60% had mania with psychosis, while 11.00% of patients presented with 1st episode mania. In our sample, 33.60% of our patients consumed 180-270 mg of caffeine/day followed by 26.40% of patients who consumed 90-180mg of caffeine /day. Overall, frequency of patients in our study who consumed caffeine more than 180mg/day, was 55.00%, with or without caffeine acting as causative triggering factor. Notably, 99.00% of our patients fulfilled the criteria for sleep disturbance, based on scores from Athens

insomnia rating scale. Additional analysis showed that 69 (62.00%) patients were black tea users followed by 22.00% who used combination of two types of caffeine. Among total participants, 35.40% consumed 4-6 caffeinated drinks/day while 3.60% consumed none or an occasional caffeinated drink per day.

Table-II: Frequency of Causative Factors in Triggering Bipolar Affective Disorder(n=110)

Causative factors identified in relapse of Bipolar affective disorder, alone and combined	n (%)
Stressors alone	20(18.20%)
Erratic adherence to medication alone	8(7.30%)
Excessive use of stimulants like caffeine alone	18(16.40%)
Stressors and erratic adherence to meds combined	6(5.50%)
Stressors and excessive use of caffeine combined	19(17.10%)
Erratic adherence and excessive use of caffeine combined	30(27.30%)
All 3 factors, combined	9(8.20%)

As shown in Table–II, 27.30% of patients had relapse of symptoms due to combined factors of erratic adherence and excessive caffeine i.e. more than 180mg use (> 4 caffeinated drinks /day during last 2 weeks) with 18% cases triggered due to stress, 17% developing the illness due to combined factor of stress and excessive caffeine use followed by 16% who relapsed due to excessive caffeine use alone. In our study population, 8% experienced symptoms of bipolar illness due to combination of stress, excessive caffeine and erratic adherence while a total of 69% of patients' disease was found to be triggered due to use of excessive caffeine alone and combined with factors of stress and non-adherence. In Table–III, among types of bipolar disease, relapse with manic episode was seen with highest frequency in almost half of female patients. Similarly, among causative factors, excessive use of stimulants like caffeine alone (16.40%) and erratic adherence combined to excessive use of caffeine (20.90%) showed similar trend of triggering relapse of manic episode in most of our patients.

In Table–VI, the highest frequency of patients developed relapse of manic episode due to consumption of 180-225mg of caffeine/day (15.50%) followed by 13.60% who experienced relapse after consuming 90-135mg of caffeine/day, indicating vulnerability of bipolar patients towards manic relapse even after moderately increased consumption of caffeine. Among other causative factors like adherence issues, surprisingly 45.40% of patients with bipolar illness were found adherent towards medication while 39.90% patients had erratic adherence.

DISCUSSION

The results of our study showed that 99.00% of our sample had insomnia which is consistent with another study which identified 69.00 to 99.00% patients with reduced need for sleep during manic episode.[1] In literature, the use of caffeine is known to cause sleep disruption that leads to relapse of mania,[7] by inducing internal susceptibility towards reduced sleep in bipolar patients.[1] A study indicated that even a single night of sleep disturbance caused relapse in 75.00% of bipolar patients.[8] This was similar to our results in which disturbed sleep, even after caffeine use of <225 mg/day, resulted in trigger of bipolar episode in 69.00% of patients. Another study confirmed the bidirectional relationship between daily use of coffee, tobacco and alcohol and disruption in sleep/wake cycle in euthymic individuals with bipolar illness,[9] while another study also indicated bidirectional relationship between sleep and affective symptoms.[10] One author recognized disturbed sleep as

Table-III: Frequency of Disease in Relation to Gender and Causative Factors (n=110)

Type of bipolar disease					Total	*p*-value
Gender	1st manic episode	Relapse of Bipolar affective disorder, Manic episode	Relapse of Bipolar affective disorder, Mania with psychosis	Mixed affective state		
Male	11(10.00%)	63(57.30%)	4(3.60%)	4(3.60%)	82(74.50%)	<0.001
Female	2(1.80%)	14(12.70%)	11(10.00%)	1(0.90%)	28(25.50%)	
Total	13(11.80%)	77(70.00%)	15(13.60%)	5(4.50%)	110(100.0%)	

Table V: Type of Bipolar Disease in Relation to Amount of Caffeine Consumed Per Day (n=110)

Total amount of caffeine per day	Type of bipolar disease				n (%)	*p*-value
	1st manic episode	Relapse of Bipolar affective disorder, Manic episode	Relapse of bipolar affective disorder, Mania with psychosis	Mixed affective state		
45 - 90 mg	1(0.90%)	9(8.20%)	6(5.50%)	0(0.00%)	16(14.50%)	< 0.001
90 - 135 mg	2(1.80%)	15(13.60%)	0(0.00%)	0(0.00%)	17(15.50%)	
135 - 180 mg	3(2.70%)	7(6.40%)	0(0.00%)	2(1.80%)	12(10.90%)	
180 - 225 mg	0(0.00%)	17(15.50%)	5(4.50%)	0(0.00%)	22(20.00%)	
225 - 270 mg	4(3.60%)	10(9.10%)	1(0.90%)	0(0.00%)	15(13.60%)	
270 - 315 mg	0(0.00%)	4(3.60%)	1(0.90%)	3(2.70%)	8(7.30%)	
315 - 360 mg	0(0.00%)	4(3.60%)	0(0.00%)	0(0.00%)	4(3.60%)	
360 - 400 mg	0(0.00%)	2(1.80%)	2(1.80%)	0(0.00%)	4(3.60%)	
More than 400mg	0(0.00%)	8(7.30%)	0(0.00%)	0(0.00%)	8(7.30%)	
Nil	3(2.70%)	1(0.90%)	0(0.00%)	0(0.00%)	4(3.60%)	
Total	13(11.80%)	77(70.00%)	15(13.60%)	5(4.50%)	110(100.00%)	

Table-VI: Type of Bipolar Disease in Relation to Adherence to Medication (n=110)

Adherence-Yes	0(0.00%)	44(40.00%)	4(3.60%)	2(1.80%)	50(45.40%)	< 0.001
Erratic/Irregular	0(0.00%)	30(27.20%)	11(10.00%)	3(2.70%)	44(39.90%)	
Not Applicable (1ST manic episode)	13(11.80%)	3(2.70%)	0(0.00%)	0(0.00%)	16(14.50%)	
Total	13(11.80%)	77(70.00%)	15(13.60%)	5(4.50%)	110(100.00%)	

common prodromal symptom of manic episode and emphasized that good sleep quality with minimal interruption can prevent the relapse and severity of manic episodes.[11] A study from Pakistan, examined the relation of caffeine consumption with excessive day time sleepiness and observed that 4.50% of students with this condition used caffeine > 4 cups/day,[12] while another study evaluated perceived negative effects of consumption of caffeine by students in which 76.80% thought it caused irritability in behavior.[13] Despite negative impact on physical and mental health, it is included among legal beverages where users do not appreciate the limitations on its intake.[14] One study reported that the higher trends of caffeine use among students, with 98.60% of medical and 97.30% of non-medical students being caffeine users.[15] A nested case control study indicated that disturbed sleep pattern, substance use and mood fluctuations were more prevalent among bipolar patients as compared to control group,[16] while another study revealed that psychiatric patients had higher caffeine consumption (31% ≥5 cups coffee/day in comparison to non-psychiatric patients (21% ≥5).[17] The cessation of caffeine use also has been implicated in remission by reverse mechanism, validated by a longitudinal case report which showed that remission of seasonal bipolar disorder, after 10 years, once caffeine use of 900-1500mg/dl, was stopped, later also helped patient in dose reduction of antipsychotics and quitting benzodiazepines. Another study discussed a patient, who had consumed caffeine 537.50 to 762.50 mg/day for 2 weeks in a form of energy drinks and coffee and developed 1st manic episode which resolved 3 weeks after quitting caffeine.[18] Our study is unique in aspect that very limited research on this topic has been conducted in this region, despite the commonality of caffeine use and strong association of caffeine use with disruption of sleep cycle and development or trigger of psychiatric symptoms, thus, emphasizing the need for prevention strategy of limiting caffeine intake in predisposed psychiatric population and inquiry of use of such stimulants in routine clinical interview in primary health facilities.

LIMITATIONS OF STUDY

Our study was limited by its small sample size due to less study duration. Further research in this area needs to be conducted using different methodology, larger sample size and extended duration of study period.

CONCLUSION

Significant association was identified between excessive consumption of caffeine, sleep disturbance and onset of bipolar disorder, mixed affective state or relapse of mania with and without psychosis.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

NS & SA: Conception, study design, drafting the manuscript, approval of the final version to be published.

AA & SU: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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