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To Study The Effectiveness Of Individualized Homeopathic Medicines In Management Of Panic Disorders In Adult Population

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ABSTRACT

Introduction:The aim of this study was to evaluate the role of individualized homoeopathic medicines in the treatment of panic attacks, specifically focusing on their effectiveness in managing symptoms and improving patient outcomes. A total of 30 patients with a history of panic attacks were included in this case series, with 29 patients showing significant improvement, while 1 patient did not experience any improvement. The study employed individualized homoeopathic treatment, with remedies selected based on the patient's unique symptoms, constitution, and mental-emotional state. Assessment was conducted through regular follow-ups, symptom analysis, and clinical evaluation..Method: Study Design: A case series study .Study Setting:. The cases for the study were be selected from OPD/ IPD of college & hospital. Cases from peripheral OPD & from health camps. Sample size: 30 cases Sampling Technique: Total 30 samples with complaints of panic attacks selected by Simple Random Sampling Technique.Result: The Common symptoms in cases were palpitations, trembling , shivering, flushes of heat, etc Maximum patients that is 10 belonged to age group "40-50 years of age,6 patients belonged to 3 1-40 years of age ,6 patients belonged to 21-30 years of age and 5 belonged to 11-20 years of`age and 3 patients belonged to age group 51-60 years age Around 89 percent of patients were male and 21 percent were female. The stress factor that contributed the most was health issues of patient(9 cases) and others are money related, family related, studies related, job related, relationship related .Around 29 patients improved and 1 were still under the individualized case study .The most indicated medicine was aconite, arsenic, argentum nitricum, and other remedies were nitric acid, phosphorous, sulphur, calcarea carb, agaricus, cannabis indica, pulsatilla, psorinum, kali carbonicum, lycopodium, bryonia, Aurum Mur, aurum met, cocculus, Asarum, calcarean Fluoricum, ignatia, sepia, natrum Mur, Gelsemium, nux vomica, Staphysagria, Capsium, silicea .The

mean score for Panic disorder severity scale before and after was 22.25 and 74,0417. The p value is less than 0.001 which is highly significantConclusion: cases were taken up randomly for the study. The total number of thirty cases were derived with the interpretation of patients suffering with psychosomatic illness (panic attacks)

Keyword: Individualized homoeopathic medicines, panic attacks, case series study

INTRODUCTION:-

Panic Attacks (PA) are defined as an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during that time four or more of 13 symptoms occur .According to DSM-5 criteria (American Psychiatric Association, 2013), a diagnosis of panic disorder (PD) requires the presence of recurrent PA and persistent worry about suffering future attacks and their consequences. Epidemiological studies report a lifetime PD prevalence rate between 1.4 and 4.1% in the adult general population. The proportion of PA is somewhat higher; the World Mental Health Survey reports the prevalence of PA without lifetime PD in high income countries to be 14.4%

Being female and experiencing early stressful life events have consistently been associated with PA and PD in young adults and the middle aged. The association with other psychosocial factors, such as being separated, divorced or widowed, or having a low educational level, is still unclear Psychiatric and physical comorbidity is frequently observed among patients with PA and PD. Depression, substance abuse and dependence, agoraphobia and suicidal behavior have been reported as related to an increased occurrence of PD.Medical conditions, such as cardiovascular or respiratory diseases, are also commonly associated with PA and PD.Despite the evidence, risk factors might have differing effects on the probability of suffering from PA and PD over the lifetime. For instance, hormone changes or psychosocial stressors in women over the lifetime might impact differently on their psychopathological vulnerability. Investigating the different impacts of several risk factors across adulthood and late life can help detect potential targets for early detection and prevention of Panic attacks[1]

Panic disorder first appeared as a specific diagnostic entity in 1980, in the third Edition of "Diagnostic and Statistical Manual of Mental Disorders" (DSM III). The classical anxiety neurosis was divided into two separate entities: panic disorder and generalized anxiety disorder, whose major criteria for distinction was based, in a simplified manner, on the presence or absence of panic attacks in the patient's history. Validity of the concept of panic disorder as a clinical and autonomous entity is now widely accepted. It is based on numerous epidemiological, phenomenological, biological, genetic and therapeutic studies that have established, that panic disorder may be clearly distinguished from other anxiety and mood disorders. However, this disorder still has unknown etiology and criteria for definition remain purely clinical. Due to the severity of panic disorder, its frequency and the fact that it is too often undiagnosed (although there are effective therapeutic strategies), efforts are fully warranted, so that patients may benefit from early diagnosis and adequate treatment[2]

OVERVIEW OF PANIC ATTACKS:-

Panic attacks are the most prevalent psychiatric illnesses in the general community, are present in 15–20% of medical clinic patients. Anxiety, defined as a subjective sense of unease, dread, or foreboding, can indicate a primary psychiatric condition or can be a component of, or reaction to, a primary medical disease.

When evaluating the anxious patient, the clinician must first determine whether the anxiety antedates or postdates a medical illness or is due to a medication side effect. Approximately one-third of patients presenting with anxiety have a medical etiology for their psychiatric symptoms, but an anxiety disorder can also present with somatic symptoms in the absence of a diagnosable medical condition3

DEFINITION :- Panic attacks describes repeated attacks of severe anxiety ,which are not restricted to any particular situation Panic disorder describes repeated attacks of severe anx- iety, which are not restricted to any particular situation or circumstances. Somatic symptoms such as chest pain, palpitations and paraesthesiae in lips and fingers are common. The symptoms are in part due involuntary over-breathing (hyperventilation).

Patients often fear they are suffering from a serious illness such as a heart attack or stroke, and may therefore seek emergency medical attention. Panic disorder is often associated with agoraphobia[4]

A sudden feeling of anxiety, fear, discomfort or uneasiness may indicate a panic episode. A panic episode occurs unexpectedly, peaks within 10 minutes and includes four or more of the following sensations at the same time:

- Skipping, racing or pounding heart
- Sweating or clammy hands
- Trembling or shaking
- Shortness of breath or difficulty breathing
- A choking feeling or lump in your throat
- Chest pain, pressure or discomfort
- Nausea or stomach problems
- Feeling dizzy, unsteady, lightheaded or faint
- Feeling strange, unreal, detached or unfamiliar
- Fear that you are losing control or going crazy
- Fear that you are dying
- Feeling tingling or numbness
- Hot flushes or chills[5]

ETIOLOGY –

Endocrine and physiological changes during “spontaneous” panic attacks

Eight patients with DSM-III-defined panic attacks were compared to four normal subjects on hormonal and physiological variables measured at six predetermined times through 24 hr and also during nine “spontaneous” attacks. Levels at predetermined times were not different, other than a reduction of urinary unconjugated epinephrine in patients. Plasma prolactin was elevated at the peak of most of the attacks and correlated with attack severity. Plasma cortisol and growth hormone, and heart rate, were elevated during some attacks, and plasma norepinephrine showed small increases. Significant plasma epinephrine changes are not Observed[6]

Multiple theories and models exist which speak to the possible etiology of the panic disorder itself. Most indicate the potential role of chemical imbalance as a major factor, including abnormalities in gamma-aminobutyric acid, cortisol, and serotonin. It is believed that genetic and environmental factor plays a role in the pathogenesis of panic disorder. Several studies show that adverse childhood conditions may lead to panic disorder in adulthood. Newer research indicates that neural circuitry may have a greater role in panic disorder whereby certain areas of the brain are hyperexcitable in individuals, and that would make them prone to developing the disorder.[7 8]

Certain factors which predispose the individual towards developing this disorder are listed below:

1. BIOLOGICAL FACTORS: The symptoms of panic disorder are related to a number of biological abnormalities in brain structure and function. Biological stimulants are being used to induce panic attacks in patients with panic disorder. Evidences indicates that abnormal regulation of brain noradrenergic systems are involved in the pathophysiology of this disorder. The autonomic nervous systems of patients have reported to exhibit the increased sympathetic tone, to adapt slowly to repeated stimuli and excessively respond to moderate stimuli.

2. PANIC-INDUCING SUBSTANCES: These are also called as panicogens, induce panic attacks in patients suffering with panic disorder. The so called respiratory panic- inducing substances causes respiratory stimulation and shift in acid-base balance. The hyperventilation in patients with panic disorder may be caused by a increased or hypersensitive suffocation alarm system. The neurochemical panic inducing substances primarily affects the noradrenergic, serotonergic and GABA receptors of the CNS directly. 3. BRAIN IMAGING: MRI in patients with panic disorder have shown pathological involvement in the temporal lobes, especially the hippocampus and the amygdala. One MRI study reported cortical atrophy in the right temporal lobe of these patients. Functional brain imaging like positron emission tomography (PET) have shown dysregulation in cerebral blood flow. Anxiety and panic disorders are associated with cerebral vasoconstriction which might result in CNS dysfunction and results in dizziness

4. GENETIC FACTORS: Studies have found that first degree relatives of patients have four to eight fold higher risk for developing this disorder than patients with some other psychiatric illness. The twin studies conducted have reported that monozygotic twins are more prone and concordant for panic disorder.

5. PSYCHOSOCIAL FACTORS: Patients with panic disorder have a higher incidence of stressful life events particularly loss9The hypothesis that stressful events produce neurophysiological changes in panic disorder is supported by the a study of female twins which shows that separation from the mother early in life was more likely to result in panic disorder than paternal separation. Another etiological factor appears to be childhood sexual abuse and physical abuse in adult female patients[10]

PREVALENCE-

The lifetime and current weighted prevalence of PD was 0.5% (95% confidence interval 0.49-0.52) and 0.3% (95% confidence interval 0.28-0.41), respectively. The male gender and unemployed have significantly lesser odds with current PD. The elderly, Urban metro, and the married/separated group have significantly higher odds with current PD

Conclusion It is the first study reporting prevalence from a nationally representative sample from the general population of India. The survey has shed light on the epidemiology and the challenges faced by those with PD which emphasizes the urgency of bridging the treatment gap. These findings are paramount to the development of more inclusive and effective mental health policies and interventions to tackle the current burden due to PD[11]

DIAGNOSIS :

The diagnostic criteria for panic disorder are outlined in the DSM-5, emphasizing the need for a thorough clinical assessment.

Challenges include differentiating panic disorder from other anxiety disorders and medical conditions[12]

Panic Disorder; Diagnosis

These are the DSM V diagnostic criteria for Panic Disorder. Please review your diagnostic assessment (Sections A and B) using this checklist. If the symptom is "clearly present" mark that box. If the symptom has been sustained for at least 1 month mark the box "sustained". Please ensure that the determining criteria (C and D) are also met. For a diagnosis of Panic Disorder, BOTH boxes in A and B must be marked. As well, items C and D must be clearly present.

Clearly Present	Sustained	
		A) Recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur: Palpitations, pounding heart, or accelerated heart rate Sweating Trembling or shaking Sensations of shortness of breath or smothering Feeling of choking Chest pain or discomfort Nausea or abdominal distress Feeling dizzy, unsteady, light-headed, or faint Chills or heat sensations Paresthesias (numbness or tingling sensations) Derealization (feelings of unreality) or depersonalization (being detached from oneself) Fear of losing control or "going crazy" Fear of dying *Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.*
		B) At least one of the attacks has been followed by 1 month (or more) of one or both of the following: 1. Persistent concern or worry about additional panic attacks or their consequences (e.g., losing control, having a heart attack, "going crazy").
		2. A significant maladaptive change in behavior related to the attacks (e.g., behaviors designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations).
	C) The disturbance is not attributable to the physiological effects of a substance (e.g. a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism, cardiopulmonary disorders).	
	D) The disturbance is not better explained by another mental disorder (e.g., the panic attacks do not occur only in response to feared social situations, as in social anxiety disorder; in response to circumscribed phonic objects or situations, as in specific phobia; in response to obsessions, as in obsessive-compulsive disorder; in response to reminders of traumatic events, as in posttraumatic stress disorder; or in response to separation from attachment figures, as in separation anxiety disorder).	

Medications that can help treat panic attacks and panic disorder include:

- a)Antidepressants: Certain antidepressant medications can make panic attacks less frequent or less severe. Healthcare providers may prescribe serotonin-selective reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs). SSRIs include fluoxetine (Prozac®) and paroxetine (Paxil®). SNRIs include duloxetine (Cymbalta®) and venlafaxine (Effexor®).

- b) Anti-anxiety medications: Providers most commonly prescribe benzodiazepines to treat and prevent panic attacks. They help with anxiety but have addiction potential, so it's important to take them with caution. These medications include alprazolam (Xanax®) and lorazepam (Ativan®)[13]

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are a type of antidepressant that doctors prescribe to treat major depressive disorder and anxiety disorders.

TCAs work by blocking the reuptake of serotonin, norepinephrine, and dopamine in the brain. This helps increase levels of these neurotransmitters to help improve mood, relieve anxiety, and decrease feelings of fatigue.

Examples of TCAs include:

- amitriptyline
- clomipramine (Anafranil)
- desipramine (Norpramin)
- doxepin (Silenor)
- imipramine (Tofranil)
- nortriptyline (Aventyl)[14]

HOMOEOPATHIC MANAGEMENT –

In organon of medicine 6th edition Dr Hahnemann explained about case taking of mental diseases in $210 to $230[15]

Homeopathic treatment also look upon person's constitution, tendencies and origin of that particular disease apart from taking symptomatology of the patient suffering from any disease. So basically homeopathic medicines tend to affect process of disease. Medicines selected after careful understanding of patient can be able to manage acute spell of the disease also. Patient can leave better life if he has opted homeopathy treatment, as medicines are totally harmless.

Agaricus, aconitum, arsenic, Gelsemium, argentum, kali ars, phosphorus, lycopodium, ignatia, Nat mur, nitric acid Are well indicated homoeopathic remedies for the treatment of panic disorder.[16 17 18]

But,an appropriate homoeopathic remedy should be administered after a thorough case taking and case understanding, on the basis of characteristic individualistic symptoms and constitution[19]

METHODOLOGY:-

1. Study Design: The case series study

2. Study Setting: Institutional OPD and Peripheral OPD

3. Study Population: 1) Cases of Panic disorder

2) Adult population

4. Sample Size: 30 Cases

5. Method of Selection of Study Subjects:

A. Inclusion Criteria:

Age Range: Typically, participants are aged between 18 and 55 years.

Symptom Severity: Individuals may need to exhibit a certain level of symptom severity to qualify for studies, ensuring that the treatment can be adequately assessed.

Language Proficiency: Participants may need to be proficient in the language of the study to ensure comprehension of treatment protocols and assessments.

B. Exclusion Criteria:

Comorbid Conditions: Individuals with significant comorbid psychiatric disorders (e.g., schizophrenia, bipolar disorder) or severe medical conditions may be excluded to isolate the effects of panic disorder treatment.

Age Limitations: Participants under 18 or over 55 years are often excluded to maintain a specific demographic focus.

C. Withdrawal Criteria:

1. Lost to follow ups
2. Not Consensual
3. DAMA/LAMA

6. Operational Definitions:

Panic disorder is a type of anxiety disorder. It causes repeated panic attacks, which are sudden periods of intense fear, discomfort, or a sense of losing control. These attacks happen even though there is no real danger. They often cause physical symptoms.

study will be carried out on adults suffering from panic disorder based on panic disorder Severity Index. All the 30 cases are given individualized homoeopathic medicines based on complete case taking.

7. Method of Measurement:

Several of the following questions refer to panic attacks and limited symptom attacks. For this questionnaire we

define a panic attack as a sudden rush of fear or discomfort accompanied by at least 4 of the symptoms listed below.

In order to qualify as a sudden rush, the symptoms must peak within 10 minutes. Episodes like panic attacks but

having fewer than 4 of the listed symptoms are called limited symptom attacks. Here are the symptoms to count:

• Rapid or pounding heartbeat

• Chest pain or discomfort

• Chills or hot flushes

• Sweating

• Nausea

• Fear of losing control

• Trembling or shaking

• Dizziness or faintness going crazy

• Breathlessness

• Feelings of unreality

• Fear of dying

• Numbness or tingling

8. Study Instruments/Data Collection Tools: MS Word, MS Excel, Case recording format

9. Method of Data Collection: Case recording format, MS Excel, MS Word

10. Data Management and Analysis Procedure: Data would be compiled in MS word and appropriate statistical tests would be applied

11. Data Analysis Plan and Methods: Paired T test

12. Outcome Assessment Criteria:

IMPROVED CASE

According to panic severity scale the difference between the composite scores of Patient before and after treatment more than or equal to 0.28 is considered to be improved case.

UNIMPROVED CASE

According to panic severity scale the difference between the composite scores of Patient before and after treatment less than or equal to 0.14 is considered to be unimproved case.

Treatment Details: Remedy was given in globules form of 40 number single dose and rubrum was given in globules form of 30 number in 1 dram bottle.

Selection of Potency: Potency is selected based on depth of pathology, severity and clarity of symptoms and predisposition of patient.

Ethical issues, if any: None

RESULT-

Statistical Analysis

Table No.1. Statistical Chart of Age Distribution-

AGE GROUP	NO. OF PATIENTS	PERCENTAGE%
11-20	5	16.67
21-30	6	20
31-40	6	20
41-50	10	33.33
51-60	3	10

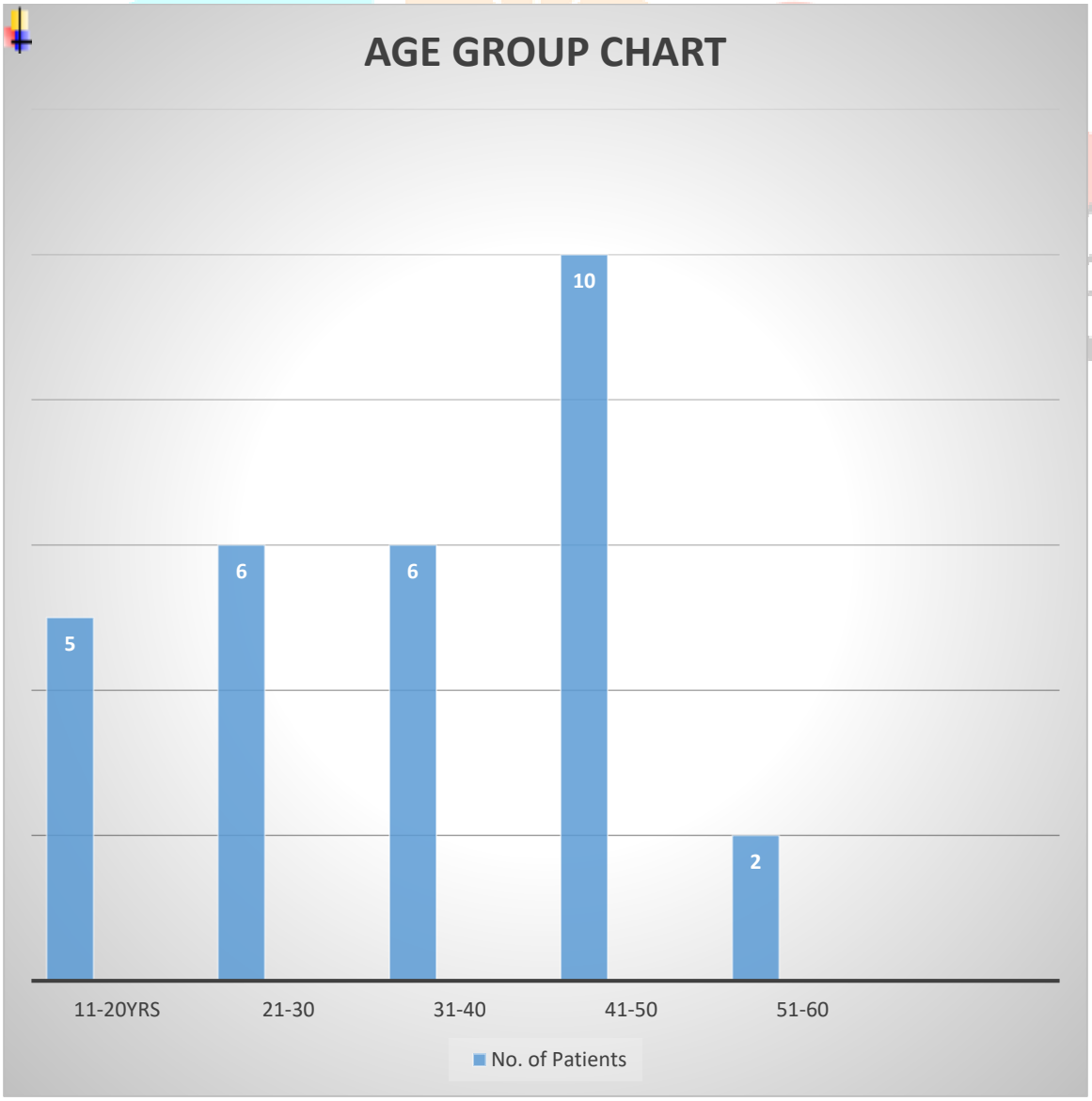


Table No.2. Statistical Chart of Sex and Marital Status

MARITAL STATUS	GENDER	FREQUENCY	PERCENTAGE(%)
MARRIED	MALE	11	36.66
	FEMALE	9	30
UNMARRIED	MALE	8	26.66
	FEMALE	2	6.66

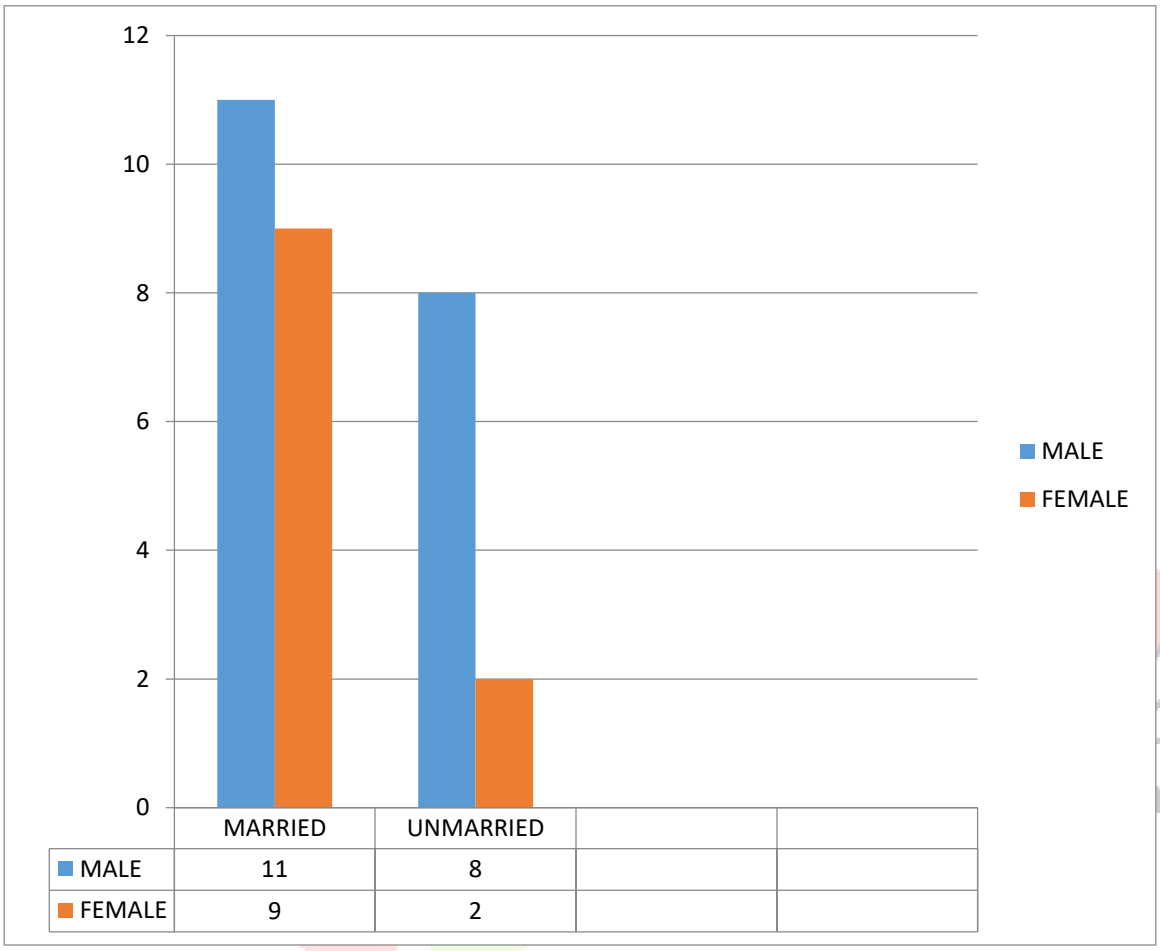


Table no.3. Statistical chart of Exciting Causes

SR.NO	EXCITING CAUSES	NO. OF PATIENTS	PERCENTAGE(%)
1	Heath about	9	30
2	Money matters	2	6.66
3	Others about	4	13.33
4	Examination related	3	10
5	Family related	3	10
6	Love disappointed	3	10
7	Busssiness related	2	6.66
8	Grief	1	3.33
9	Menopause	1	3.33
10	Studies related	1	3.33
11	Job related	1	3.33

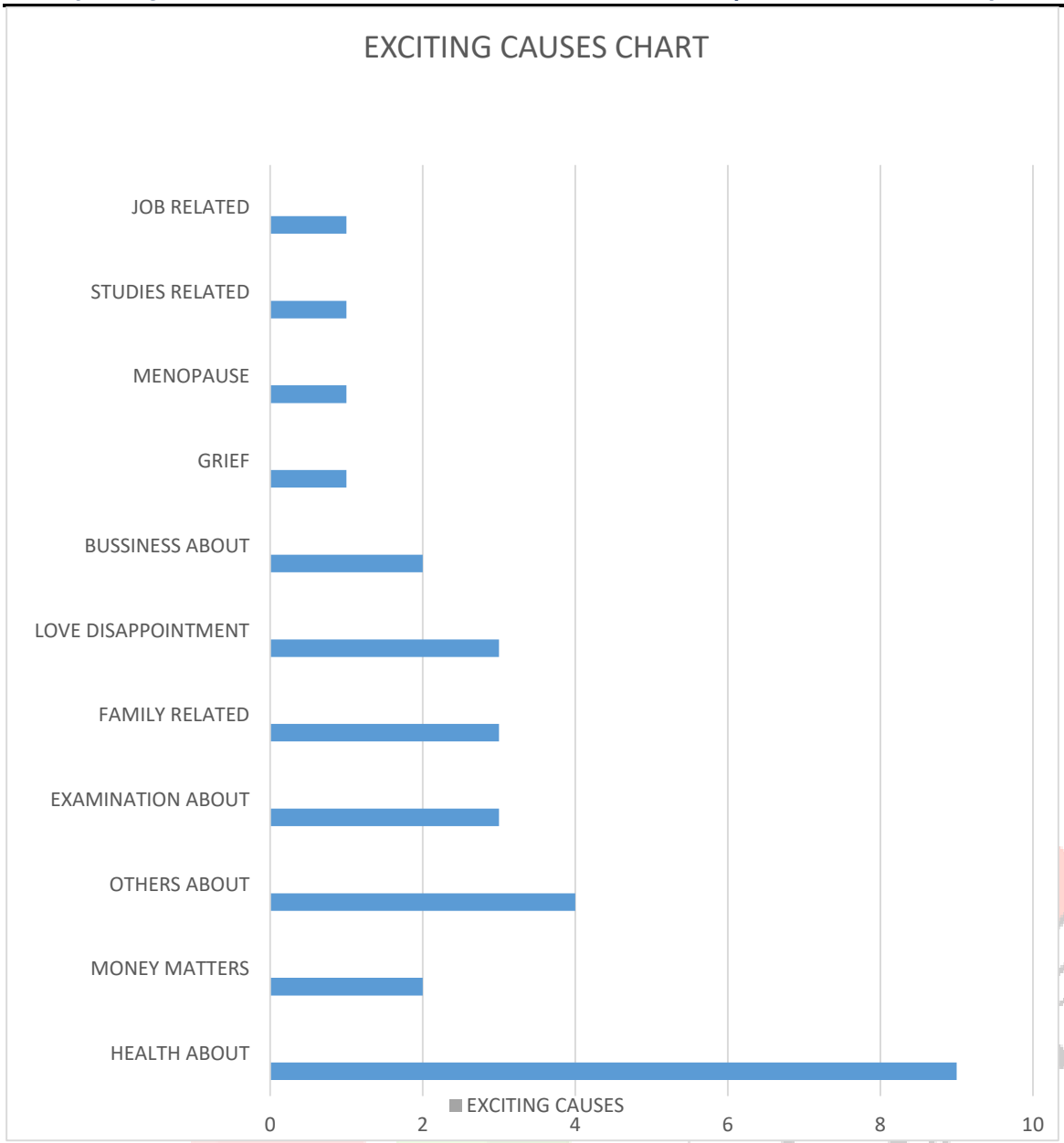


Table No.4. Statistical Chart of Remedies Prescribed

SR.NO	REMEDIES	NO. OF PATIENTS TAKEN	PERCENTAGE(%)
1	Nitric acid	1	3.33
2	Phosphorus	1	3.33
3	Calcarea carb	1	3.33
4	Sulphur	1	3.33
5	Agaricus	1	3.33
6	Aconite	2	6.66
7	Arsenic album	2	6.66
8	Argentum nitricum	2	6.66
9	Cannabis indica	1	3.33
10	Pulsatilla	1	3.33
11	Psorinum	1	3.33
12	Kali carbonicum	1	3.33
13	Lycopodium	1	3.33
14	Bryonia	1	3.33

15	Aurum mur	1	3.33
16	Aurum met	1	3.33
17	Cocculus	1	3.33
18	Asarum	1	3.33
19	Calcarea fluoricum	1	3.33
20	Ignatia	1	3.33
21	Sepia	1	3.33
22	Natrum mur	1	3.33
23	Gelsemium	1	3.33
24	Nux vomica	1	3.33
25	Staphysagria	1	3.33
26	Capsicum	1	3.33
27	Silicea	1	3.33

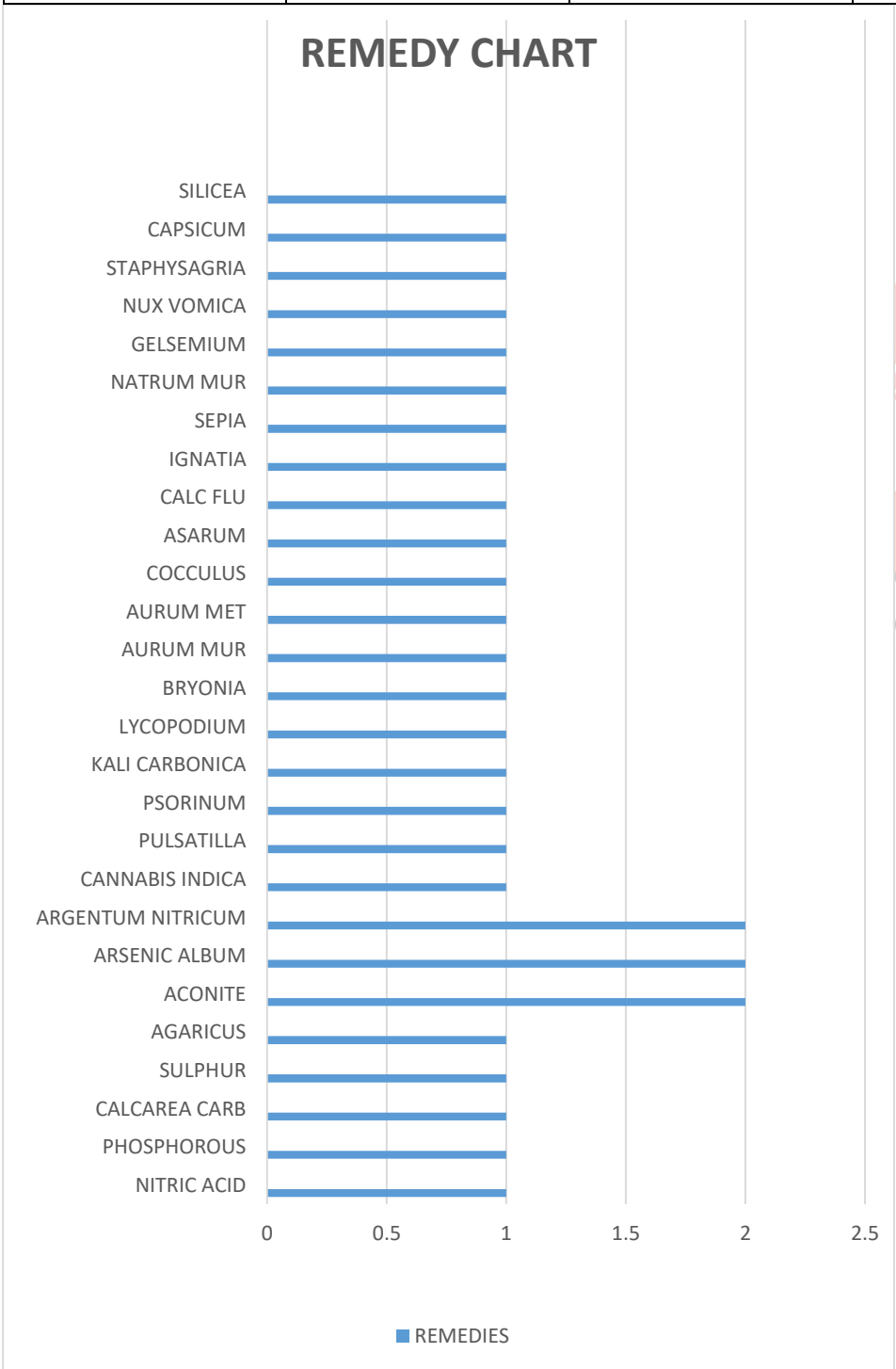


Table No.5. Statistical chart of Distribution of Potency

POTENCY	NO. OF PATIENTS	PERCENTAGE(%)
30 C	2	6.66
200 C	14	46.66
1 M	14	46.66

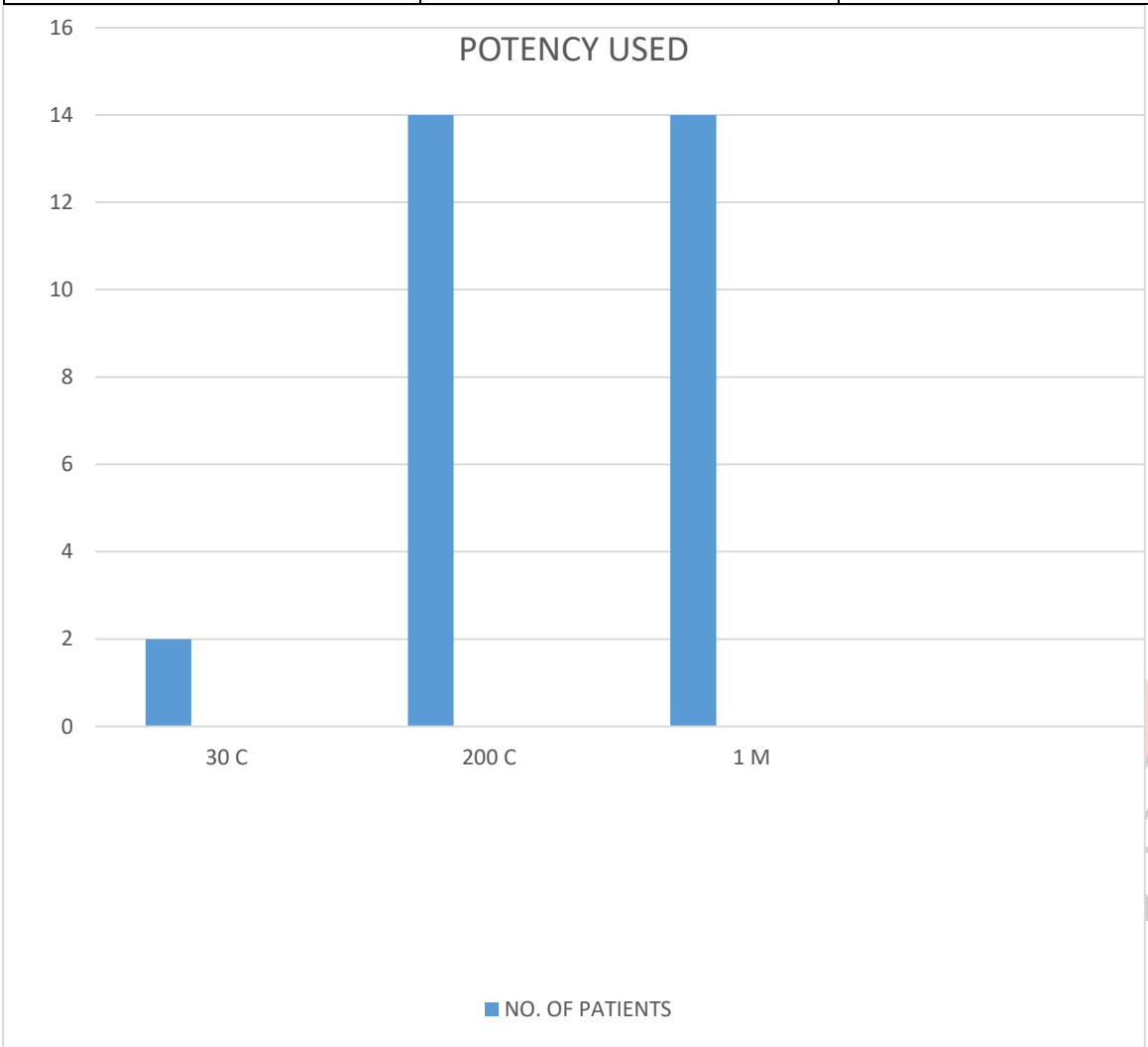
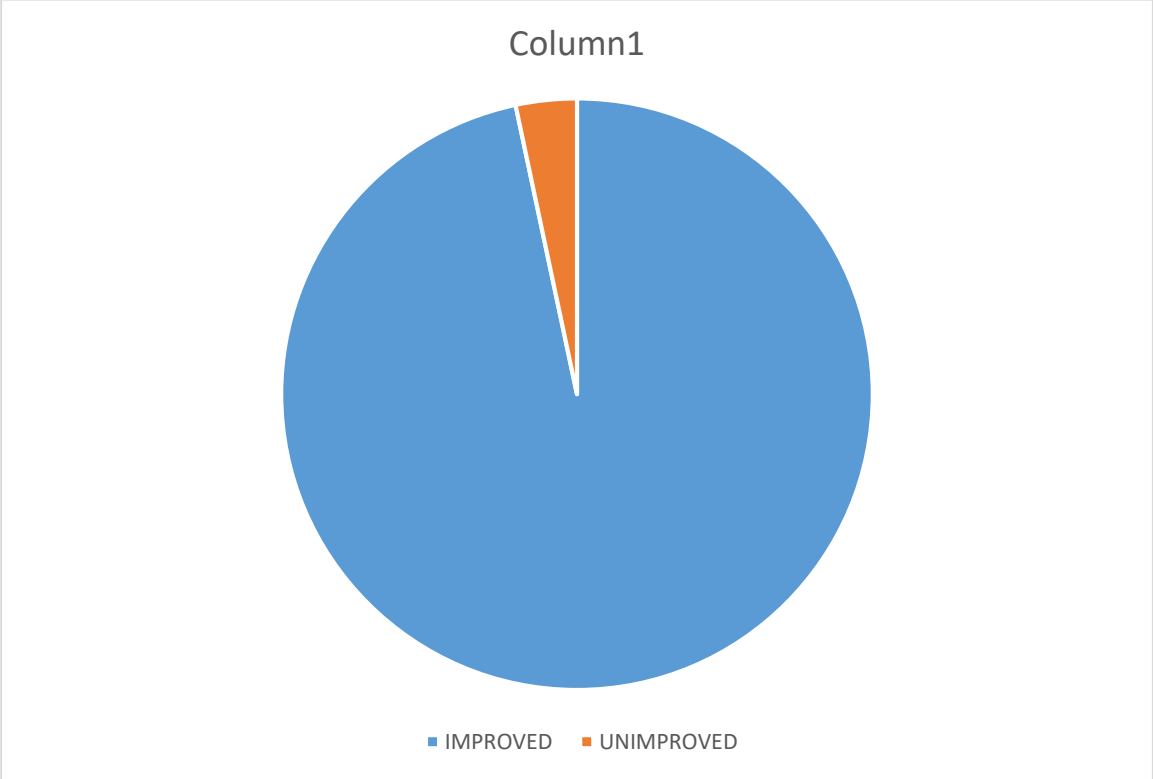


Table No.6. Statistical chart of Result of Treatment

RESULT	FREQUENCY	PERCENTAGE(%)
IMPROVED(I)	29	96.66
NOT IMPROVED(NI)	1	3.33



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UNIMPROVED CASE

According to panic severity scale the difference between the composite scores of Patient before and after treatment less than or equal to 0.14 is considered to be unimproved case.

The value of t=15.96

determine the critical values for t with degrees of freedom=15 and $\propto = 0.05$

in this critical value is 1.753 (see the table below)

the calculated t exceeds the critical value (15.96>1.753),so the means are significantly different

DISCUSSION:-

The present study aimed to explore the role of individualized homoeopathic treatment in the management of panic attacks. The case series included 30 patients diagnosed with panic disorder, of whom 29 showed improvement, while 1 patient did not respond positively to the treatment. The findings suggest that individualized homoeopathic medicines may have a significant role in alleviating the symptoms of panic attacks, particularly when treatment is tailored to the individual's unique constitutional and symptomatological profile.Efficacy of Individualized Homoeopathic Treatment -Out of the 30 patients treated, 29 (96.7%) experienced marked improvement, with a reduction in the frequency, intensity, and duration of panic attacks. This high rate of improvement is consistent with previous studies that have shown homoeopathy to be effective in treating a variety of psychiatric disorders, including anxiety and panic attacks The individualized approach in homoeopathy, where remedies are selected based on the totality of symptoms, including physical, emotional, and psychological aspects, may have contributed to this positive outcome.Panic disorder is often a complex condition with multifactorial causes, including genetic, environmental, and psychological factors. The individualized treatment strategy in homoeopathy takes into account not only the presenting symptoms but also the patient's overall health, emotional state, and past medical history. This holistic approach appears to have

contributed to the improvement observed in the majority of patients in this study.The Case of Non-Improvement-While the overwhelming majority of patients experienced improvement, one patient did not respond to treatment. It is important to acknowledge that homoeopathic treatment may not always yield favorable results for every patient. Non-improvement in this case could be attributed to various factors, including the possibility of an incorrect remedy prescription, the patient's specific constitutional factors, or the complexity of the underlying psychological issues, which might require more prolonged or different therapeutic approaches. The one patient who did not improve may also represent the need for more comprehensive or integrative treatments, including psychotherapy or other medical interventions, especially in cases where panic attacks are part of a more complicated or severe mental health condition.Homoeopathic Principles in Treating Panic Attacks-According to homoeopathic principles, the selection of a remedy is based on the totality of symptoms, which includes the mental, emotional, and physical symptoms experienced by the patient. In the case of panic attacks, the mental and emotional symptoms are particularly important, as the experience of fear, anxiety, and a sense of impending doom is central to the disorder. Remedies such as Arsenicum album, Aconite, and Gelsemium, which are commonly used to treat anxiety and panic attacks, were likely selected based on the individual symptom profiles of each patient. This individualized approach aligns with the philosophy of homoeopathy, where the aim is not just to suppress symptoms but to stimulate the body's innate healing mechanisms. The results from this study suggest that when the correct remedy is selected, the body can rebalance itself, leading to long-term symptom relief.Limitations and Future Directions-While the results are promising, it is important to note the limitations of this study. The sample size of 30 patients is relatively small, and the study lacks a control group for comparison. Additionally, the follow-up duration was not specified, and it is crucial to assess the long-term effects of homoeopathic treatment on panic attacks. A larger, randomized controlled trial would provide stronger evidence regarding the efficacy of individualized homoeopathy in treating panic attacks.Another limitation is the subjective nature of symptom assessment in panic disorder. Although clinical improvement was observed in the majority of patients, the assessment relied heavily on patient-reported outcomes, which may introduce bias. Objective measures such as standardized anxiety scales or physiological markers of anxiety would provide a more comprehensive evaluation of the treatment's impact.

CONCLUSION:-

Cases were taken up randomly for the study. The total number of thirty cases were derived with the interpretation of patients suffering with psychosomatic illness (panic attacks)

The following conclusions were drawn from the study.

1. The prevalence of panic attacks is found predominantly among males (19 cases) and less in females (11 cases).

2. Majority of patients belonged to the age group of 40-50 years that is 10cases.

3 Majority of patients suffering belonged to the Hindu community

4. Most of the patients who are suffering are married 20 cases

5. It is found that the panic attacks was most frequently seen among the

middle socioeconomic group

6. The stress factor that contributed the most was health issues of patient (9 cases) and others are money related, family related, studies related, job related, relationship related.

7. Almost in every case the prescription is formed based on individualized case taking.

8. Among the thirty cases treated, most of the cases required 1M Potency (16 cases) and 200C (14 cases) and remaining cases needed 30C (2 cases).

9.The repetition schedule followed was only repetition in 1 cases otherwise remaining cases were better with first prescription.

10.The susceptibility found to be in most of the cases is high 16 cases.

11.Around 29 patients improved and 1 were still under the individualized case study .

Conflict of Interest- None

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