

**ABSTRACT** Generalized anxiety disorder(GAD) is mainly characterized by a dysfunction in the serotonergic system leading to excessive, persistent anxiety and unnecessary worry about everyday life.WHO reported that anxiety disorders ranked sixth place among all mental illnesses. This review mainly focuses on the research of diagnostic criteria, pharmacological therapy, cognitive behavioral therapy, and lifestyle measures in GAD. A GAD study of Scandinavian patients demonstrated prevalence rates of females(6%) are twice that of males(4.8%).GAD-7 scale is the standardized set of tools for diagnosing and screening anxiety disorders.SSRI and SNRI are the most frequently prescribed class of medications for therapeutic management of GAD. Cognitive-behavioral therapy(CBT) is an education platform that plays a crucial role by guiding patients in managing GAD. Few research studies also showed that kundalini yoga is also useful in controlling anxiety symptoms. Breathing exercises, meditation, and practicing postures help to relieve somatic symptoms. However, antidepressants along with CBT are the first-line therapy for GAD management. Anxiety when untreated may result in the development of serious comorbidities like Depression and bipolar disorders. So, patients must be counseled and educated by clinical psychologists, pharmacists, and other health care professionals regarding their lifestyle modifications and mental illness for self-management.

**KEYWORDS**: Generalized anxiety disorder, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, cognitive behavioral therapy, kundalini yoga.

### INTRODUCTION

Generalized anxiety disorder(GAD) is mainly characterized by a dysfunction in the serotonergic system leading to excessive, persistent anxiety and unnecessary worry about everyday life. It is also associated with impairment in functioning, interpersonal problems, and increased utilization of medical services<sup>[1]</sup>.GAD differs from normal anxiety<sup>[2]</sup>.

## EPIDEMIOLOGY

Childhood anxiety occurs in about 4 children between the age of 13 and 18 years. the median age of onset is 11 years. however, the lifetime prevalence of a severe anxiety disorder in children is approximately 6  $\%^{[3]}$ . The NESARC study on GAD showed a lifetime prevalence of 2.1%. But these are lower than the earlier NCS, which showed a lifetime prevalence of 5.1%. According to a study from Scandinavian patients, prevalence rates of GAD showed that females(6%) demonstrated twice than males(4.8%)<sup>[4]</sup>. In 2015, WHO reported that Anxiety disorders ranked sixth place among all mental illnesses.

### ETIOLOGY

Many factors are contributing to developing GAD. An interaction of biopsychosocial factors such as stress, comorbidities, genetic vulnerability(first degree relatives with GAD-25%), environmental factors, and substance abuse may cause anxiety. Among them, the first-ever factor is negative life events. occurrence of more negative events may lead to an increased risk of acquiring GAD<sup>[5]</sup>.

Post-traumatic stress disorder is one of the most experienced factors leading to anxiety. This type of event may cause intrusive thoughts, psychic numbing, hyperarousal, and sleep disturbances<sup>[6]</sup>.

Another major factor contributing to GAD is genes. Epistatic interaction of S-5-HTTLPR and the BDNF-Met predispose may cause epigenetic aberrations leading to anxiety<sup>[7]</sup>.

## Clinical Features And Diagnostic Criteria-(DSM-V)

The American psychiatric association is the first one to introduce the diagnosis of GAD in the DSM-III. Later additional changes were made and updated versions of DSM-IV and DSM-V were released.

According to the Diagnostic and statistical manual of mental disorder, fifth edition, the diagnostic criteria for GAD are mentioned in Table 1<sup>[8]</sup>. Anxiety may also result in distress or Impairment in social and occupational areas<sup>[4]</sup>.

# Table 1: Diagnostic Criteria For Generalised Anxiety Disorder

Excessive anxiety and worry(apprehensive expectation),occuring more days than not for at least 6 months,about a number of events or activities(such as work or school performance) 2 The indivisual finds it difficult to control the worry.

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3 The anxiety and worry are associated with three(or more) of the following symptoms(with atleastsome symptoms having been prsent for more days than not for the past few months): Note:

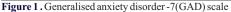
- A. Restlessness or feeling keyed up or on edge
- B. Being easily fatigued.
- C. Difficulty concentrating or mind going blank.
- D. Irritability.
- E. Muscle tension.

F. Sleep disturbance(difficulty falling or staying asleep, or restlesness, unsatisfying sleep).

- 4 The anxiety, worry or physical symptoms cause clinically significant bdistress or impairment in social, occupational or other important areas of functioning
- 5 The distrubence 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).
- 6 The distrubence is not better explained by another mental disorder(e.g, anxiety or worry about having panic attacks in panic disorder, negitive evaluation in social anxiety disorder(social phobia, contamination or ther obesessions in obsessive-compulsive disorder, seperation from attachment figures in seperation anxiety disorders, reminders of traumatic events in post traumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptoms disorder, nerviced appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder or the content of delusional beliefs in schizopherenia or delusional disorder).

The generalized anxiety disorder scale(GAD-7) is one of the most standardized set of tools used for screening and diagnosing anxiety disorder. Figure 1 shows seven standard set of self-report questionaries that are used in evaluating the severity of anxiety.

Over the last 2 weeks, how often have you been bothered by the following problems?		n Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge		0	1	2	3
2. Not being able to stop or control worrying		0	1	2	3
3. Worrying too much about different things		0	1	2	3
4. Trouble relaxing		0	1	2	3
5. Being so restless that it is hard to sit still		0	1	2	3
6. Becoming easily annoyed or irritable		0	1	2	3
7. Feeling afraid as if something awful might happen		ippen 0	1	2	3
to do your work, take o	Total Score problems, how <u>difficult</u> I are of things at home, o	r get along	with othe	r people?	10.55
Not difficult at all	Somewhat	Very difficult			



### HEALTH CARE MEASURES

Scoring and interpretation are done by questioning the patients to rate the frequency of symptoms in the last two weeks on a Likert scale which ranges from 0-3(0-not at all;1-more than half days;1-several days;2-nearly every day). If the cut-off point is 10 or greater, sensitivity and specificity exceed 0.80.GAD patients have a sensitivity of 89% with a cut of point of 10 or above. Whereas the ones having lesser than 10 are without GAD. The total score is calculated by summing up the individual scores of 7 questions.5,10 and 15 are the cut-off points for mild, moderate, and severe anxiety respectively<sup>[9]</sup>.

### TREATMENTS FOR GENERALISED ANXIETY DISORDER

Selective serotonin reuptake inhibitors(SSRI'S) and serotoninnorepinephrine reuptake inhibitors(SNRI'S)

SSRI and SNRS are the most widely prescribed first-line drugs for the treatment of anxiety disorder. They mainly inhibit the reuptake of serotonin and norepinephrine., leading to increased levels of serotonin in the synaptic cleft<sup>[10]</sup>. Fluoxetine is useful for reducing anxiety symptoms in youth. A study showed that 61% of patients who were on fluoxetine have shown well tolerable effects compared to the ones in placebo. But many have experienced mild headaches and gastrointestinal side effects<sup>[11]</sup>.

Paroxetine is one of the most beneficial and efficacious medications used for short-term therapy of GAD. In a double-blind, placebocontrolled study, 68% and 80% of patients treated with 20mg/40mg of paroxetine showed promising results in controlling anxiety symptoms, when compared with 52% of placebo patients. There were at least some patients in the placebo group who reported adverse events during the treatment period. Asthenia, constipation, dry mouth, abnormal ejaculation, somnolescence, decreased appetite, sweating, yawning and female genital disorders are the adverse events that were experienced by the placebo patients. there were no severe events. The mild and moderate events are diminished over the treatment period<sup>[12]</sup>.

#### **Benzodiazepines**

Benzodiazepines are among the most widely prescribed medications for the treatment of anxiety disorder. Majorly, they are preferred for short-term treatment why because long-term therapy produces side effects like sedation, cognitive impairment, etc<sup>[13]</sup>, studies of benzodiazepines have shown that patients on clonazepam experienced lesser side effects when compared to lorazepam and alprazolam. This beneficial effect of clonazepam is due to its lower lipid solubility and slow elimination half-life. Benzodiazepine's in combination with an antidepressant could be an efficacious treatment for GAD<sup>[14]</sup>

#### Cognitive Behavioural Therapy(CBT)

Cognitive-behavioral therapy emerged in the late 1950s for the treatment of psychopathology<sup>[15]</sup>.CBT is one of the most frequently used therapy for anxiety disorders. Therapy includes both cognitive and behavioral training sessions for 4 months. It mainly focuses on controlling negative thoughts, feelings, behaviors, and excessive worrying<sup>[16]</sup>.

Digital CBT is another mode of therapy that is held through apps via smartphones. This is cost-effective and beneficial. In this intervention, a virtual therapist asks the patients online about their anxiety. For the intervention of GAD therapy, evidence-based CBT techniques like psychoeducation, stimulus control, applied relaxation, cognitive restructuring, and self-monitoring are used. The outcomes are measured with help of the GAD-7 scale[17]

yoga is one of the which have beneficial effects on mental health. It helps in managing anxiety, stress, negative feelings, and insomnia. It induces the development of the human body, structural, physiological, and psychological effects.

Kundalini yoga showed potential therapeutic benefits in relieving anxiety symptoms by practicing mediation, breathing exercises, and physical postures. Mind-body practices control the mind and decrease somatic symptoms<sup>[18]</sup>.

A randomized clinical trial of yoga efficacy on GAD showed that 54.2% of participants who practiced kundalini yoga resulted in promising effects than the ones in the stress education group(33%). These results concluded that Kundalini yoga is more efficacious for GAD therapy but not as beneficial as CBT.CBT along with antidepressants is the first-line therapy for Generalized anxiety disorder<sup>[19]</sup>

GAD can be managed properly if the patients are properly counseled and educated by clinical psychologists, pharmacists, and health care professionals regarding mental illness and lifestyle<sup>[20]</sup>. For good medication compliance, a family should be supportive in all possible measures. Anxiety when untreated may lead to the development of serious comorbidities like depression and bipolar disorder. So, patients must modify their lifestyle and include yoga in daily life for better outcomes. Agents like caffeine, cocaine, nicotine, and alcohol induce anxiety. They must be avoided. Although the pharmacological therapy currently using is beneficial, it has several side effects. CBT is an education platform that plays a vital role in guiding patients and helpful in controlling anxiety symptoms.

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