

REVIEW ARTICLE

Generalized anxiety disorder: a review

Yazed Khalid Alkhader^{1*}

ABSTRACT

Generalized anxiety disorder is an anxiety subtype, it is an excessive concern and stress about complications on most days and it persists for at least 6 months. Prevalence of the disease differs among different studies according to the study population and considered criteria. Risk factors and symptoms were studied for the disease, however, it is mostly misdiagnosed with depression, hence, it is necessary to take proper history of the patient and investigate well before final diagnosis. Treatment of the disease involves drugs, several psychological therapies, out of which the most effective one is cognitive behavior therapy.

Keywords: GAD, GAD prevalence, GAD diagnosis, psychological therapies.

Introduction

Anxiety disorder is an emotion which is characterized by feelings of worried thoughts, tension, and physical changes such as increased blood pressure [1]. There are several forms of anxiety including generalized anxiety disorder (GAD), social anxiety disorder, panic disorder, and specific phobias [2]. GAD is an extravagant tension and worry about daily calamities and problems on most days, it lasts for at least 24 weeks, where the person experiences difficulty in performing day to day tasks [3]. GAD is characterized by autonomic hyperactivity, increased motor tension, and increased vigilance and scanning with lacking of panic attacks [3]. It was reported that the spread of GAD ranged from 1.5% to 3% among adults [4]. In the current review, we aimed to overview the GAD.

Materials and Methods

We searched scientific websites such as ResearchGate, Google Scholar, and PubMed. With the keywords including; GAD, prevalence of GAD, treatment of GAD, and risk factors for GAD. We collected 18 articles, six of them were included which were published between 2002 and 2017, while the other articles were excluded because they weren't focusing on the current subject.

GAD and its prevalence

GAD was first identified in the Diagnostic and Statistical Manual of Mental disorders (DSM-III). GAD was defined by DSM-III as 4 weeks of persistent anxiety which was associated with symptoms from three of four categories [5]. DSM-III-R varied the requirements of worry to make the validity of separation better from normal anxiety to 24 weeks along with 6 of 18 accompanied symptoms [6]. GAD can be defined as a constant and often intense mental disorder of the anxiety

series which is characterized by continuous anxiety for 24 weeks or more, extravagant worrying, stress accompanied with symptoms of hypervigilance, and other somatic symptoms of anxiety [7]. It was reported that the prevalence of GAD was ranged from 1.5% to 3% among adults [4], and it was suggested that 38% of individuals with GAD had comorbid personality disease [8], while 17% only had GAD alone [9]. One study from the US reported that 5% of persons will suffer GAD at time during their lives [10]. GAD develops during early adulthood and late adolescent with an average of 25–30 years for the first manifestation [11]. It was stated that based on both DSM-III and DSM-III-R, the lifetime and prevalence of GAD in general population were estimated to range from 4% to 7% and the 1-year prevalence ranges from 3% to 5% [12]. Another study reported 1-year prevalence range of 0.15%–12.7% in Northern Ireland [13] and in Christchurch, New Zealand [14], respectively. Lifetime prevalence rate was 1.9% in Basle, Switzerland [15]. A study from USA reported lifetime prevalence of 5.7% in the study sample and this rate was reported in other countries [16]. Whereas lifetime prevalence was reported to be 0.8% regarding both genders [12]. The incidence of GAD among women is double than that of men [17] and it is higher in younger persons [18]. Higher prevalence of 7.7% was reported in individuals with age range of 45%–59%, with more incidence in females (7%) than in males (4%) [19].

Correspondence to: Yazed Khalid Alkhader

*Arabian Gulf University, Manama, Bahrain.

Email: zo0ozo0o_91@hotmail.com

Full list of author information is available at the end of the article.

Received: 18 February 2018 | **Accepted:** 11 March 2018

Risk factors and symptoms of GAD

Development of GAD is dependent on both environmental and genetic factors [20]. GAD was believed to be independent of demographic factors and was related to a growing number of a few stressors [21,22], however, this was common in individuals with other diagnoses [23]. Genetic factors have a role in GAD, one systematic review reported a significant correlation among GAD in the index cases and in their relatives of first degree [24]. In a case-control association study, it was demonstrated that polymorphic variance at the receptor gene of serotonin 1-A was linked to GAD and the common clinical display of comorbid major depression [25]. Marital status, employed status, and being a homemaker were predictors for GAD [19]. Other risk factors were reported in children-based study followed into adulthood, and these factors included internalizing problems, conduction problems in childhood, low socioeconomic status, and childhood maltreatment [26]. GAD also associated with reduced quality of life and serious disability. In an international study of disability caused by mental illness, it was found that 38% of individuals suffering from GAD had intermediate to intense occupational role impairment and they missed their work with a mean of 6.3 days per month [27]. GAD is described by increased concern and display of physiological arousals such as insomnia, restlessness, and muscle tension [20]. Besides worry, patients should suffer at least three of the six physiological arousal displays which are listed in the box and they must be caused by GAD and not by medical illness, another psychiatric issue, or the medication use. Also, the symptoms have to result in impairment or serious distress for the clinical diagnosis to be done [20]. GAD symptoms were described by the international classification of diseases, 10th revision differently. It focused on physiological arousal such as palpitations, shaking, sweating, and vertigo without any requirement for symptoms presentation for 6 months [20]. It was suggested by clinical records that less than 20% of GAD sufferers experience full reduction of their display, while typically patients will have had their symptoms for a period range from 5 to 10 years previous to their diagnosed and efficient treatment [28–30].

GAD diagnosis, assessment tools, and co-morbidities

GAD patients were found to frequently use primary care purses instead of rational health specialist settings and they were related to excess usage of general health care resources [31–34]. GAD sometimes is mistaken in diagnosis in primary care as there might be a misdiagnosis of anxiety as depression [20]. In a large research [34], the primary care physicians misdiagnosed GAD in 66%, another report showed that 27% of patients who had false positive diagnosis of depression, had actually an anxiety disorder [35]. Patients suffering

from GAD often have physical presentations, and it may be hard to recognize the symptoms which are associated with medical diseases from that which are related to anxiety [28]. Practitioners have to record a history and make a physical check before making a diagnosis of GAD to set aside medical reasons of anxiety. Laboratory investigations have to be guided by the clinical symptoms [36]. Assessing GAD requires considering of medical conditions (pulmonary, neurologic, cardiac, or endocrine disorders), usage of drugs such as cocaine or stimulants such as caffeine, prescribed and over-the-counter drugs (corticosteroids and herbal medicines) and drug withdrawal (stopping the use of opiates, alcohol, or benzodiazepines) for the individuals [37,38]. It was found that 90% of individuals suffering from GAD had a comorbid diagnosis involving depression, dysthymia, bipolar disorder, substance abuse somatization, and other anxiety disorders [39]. It was found that psychiatric comorbidity was common in GAD, where 29%–62% of patients were found to complain major depression [19,34]. Social anxiety disorder represented 34%, while alcohol abuse represented 38% of GAD co-morbidities [40]. Complaining of GAD assess in the progression of major depression [20], where it was reported from large prospective research of adults and adolescent that GAD resulted in an increasing odds of depression progression within four years to a 4.5-fold [41]. Patients with comorbid psychiatric disorders are less prone to have effective reaction to treatment and more impaired than those with GAD alone [40].

GAD treatment

The treatment strategies involve drugs and psychological therapies [20]. Drugs include antidepressants, the anticonvulsant pregabalin, and benzodiazepines, while psychological therapies include behavioral therapy, cognitive behavioral therapy (CBT), relaxation response, and mindfulness meditation training [20]. It isn't known what should be tried first either psychotherapy or drugs, one study showed priority of CBT over drugs [42], while another showed an advantage of drugs such as sertraline, over CBT [43]. Also, it is unclear whether the combination of the two strategies or using only one of them is better, discussion with patients will help to choose the best option regarding patient's values, attitudes, beliefs, and resources [20]. In the current review, psychological therapies will be focused. Behavioral therapy is hard to be applied on GAD patients than in patients with simple phobias as it is more difficult to target worry of GAD [20]. CBT is the most commonly used and well studied therapy, it is provided by a specially trained psychotherapist [20], this therapy depends on teaching patients to replace positive ideas for anxiety-provoking ones, it usually involves 6–12 individual periods at week's intervals [36]. Significant benefit of CBT was reported in several meta analyses [44–46], and one randomized controlled study showed that 32% of patients who received CBT had significant

clinical improvements in 3 months, while 42% had significant improvements in 6 months [47]. This strategy traditionally combines both cognitive therapies with behavioral therapy, cognitive therapy focuses on understanding self-perpetuated cognitive distortions, monitoring thoughts, and habitual thought patterns as well as ulterior behaviors, while behavioral therapy aims to present the patient to feared situations [20]. It was suggested that CBT can be provided via the Internet, and there was an evidence of the effectiveness of Internet-based CBT managed by a non-clinician [48]. CBT can be combined with several other psychotherapeutic approaches such as relaxation response training in the form of diaphragmatic breathing or progressive muscle relaxation [20]. Relaxation therapy involves patient imagination to calm situations to stimulate both muscular and mental relaxation [36]. Two randomized controlled studies with small to medium size compared cognitive therapy alone with relaxation training alone and it was demonstrated that both equally and significantly reduced anxiety displays in GAD [49,50]. Mindfulness was introduced out of meditation training ways such as mindfulness-based stress reduction in mental health treatment settings. Mindfulness educates individuals to raise their knowledge about the present minute situations, such as emotions and thoughts, without striving or judgment to make the experience last or vanish [20].

Conclusion

GAD differs in prevalence according to the studied population. There are several environmental and genetic factors that act as risk factors for the disease. Misdiagnosis was found in primary care settings, so it is important to perform enough tests and take patients' history before confirming the case. The most effective psychological treatment approach for the disease was CBT.

Acknowledgement

None.

List of abbreviations

CBT Cognitive behavioral therapy
DSM Diagnostic and Statistical Manual
GAD Generalized anxiety disorder

Funding

None

Conflict of Interests

None

Consent for publication

Not applicable.

Ethical approval

Not applicable.

Author details

Yazed Khalid Alkhader¹

1. Arabian Gulf University, Manama, Bahrain

References

1. Alzahrani M, Alfahaid F, Almansour M, Alghamdi T, Ansari T, Sami W, et al. Prevalence of generalized anxiety disorder and major depression in health-care givers of disabled patients in Majmaah and Shaqra cities, Kingdom of Saudi Arabia. *Int J Health Sci* 2017; 11(3):9–13.
2. Dew MA, Myaskovsky L, DiMartini AF, Switzer GE, Schulberg HC, Kormos RL. Onset, timing and risk for depression and anxiety in family caregivers to heart transplant recipients. *Psychol Med* 2004; 34:1065–82.
3. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
4. Kessler RD, Wittchen HU. Patterns and correlates of generalized anxiety disorder in community samples. *J Clin Psychiatry* 2002; 63:4–10.
5. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3rd ed. Washington, DC: American Psychiatric Association; 1980.
6. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3rd ed. Washington, DC: American Psychiatric Association; 1987.
7. Wittchen HU. Generalized anxiety disorder: prevalence, burden, and cost to society. *Depress Anxiety* 2002; 16:162–71.
8. Dyck IR, Phillips KA, Warshaw MG, Dolan RT, Shea MT, Stout RL, et al. Patterns of personality pathology in patients with generalized anxiety disorder, panic disorder with and without agoraphobia, and social phobia. *J Personal Disord* 2001; 15:60–71.
9. Goldenberg IM, White K, Yonkers K, Reich J, Warshaw MG, Goisman RM, et al. The infrequency of "pure culture" diagnoses among the anxiety disorders. *J Clin Psych* 1996; 57:528–33.
10. Andrews G, Peters L, Guzman AM, Bird K. A comparison of two structured diagnostic interviews: CIDI and SCAN. *Aust N Z J Psychiatry* 1995; 29:124–32.
11. Michael T, Zetsche U, Margraf J. Epidemiology of anxiety disorders. *Psychiatry* 2007; 6(4):136–42.
12. Hoyer J, Becker ES, Margraf J. Generalized anxiety disorder and clinical worry episodes in young women. *Psychol Med* 2002; 32:1227–37.
13. McConnell P, Bebbington P, McClelland R, Gillespie K, Houghton S. Prevalence of psychiatric disorder and the need for psychiatric care in Northern Ireland. Population study in the District of Derry. *Br J Psychiatry* 2002; 181:214–9.
14. Oakley-Browne MA, Joyce PR, Wells E, Bushnell JA, Hornblow AR. Christchurch psychiatric epidemiology study, Part II: six month and other period prevalences of specific psychiatric disorders. *Aust N Z J Psychiatry* 1989; 23:327–40.
15. Wacker HR, Mulleijans R, Klein KH, Battegay R. Identification of cases of anxiety disorders and affective disorders in the community according to ICD-10 and DSM-III-R by using the Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res* 1992; 2:91–100.

16. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry* 2005; 62:593–602.
17. Seivewright N, Tyrer P, Ferguson B, Murphy S, Johnson T. Longitudinal study of the influence of life events and personality status on diagnostic change in three neurotic disorders. *Depress Anxiety* 2000; 11:105–13.
18. Pigott T. Gender differences in the epidemiology and treatment of anxiety disorders. *J Clin Psychiatry* 1999; 60:4–15.
19. Wittchen HU, Zhao S, Kessler RC, Eaton WW. DSM-III-R generalized anxiety disorder in the national comorbidity survey. *Arch Gen Psychiatry* 1994; 51:355–64.
20. Hog EA, Ivkovic A, Fricchione GL. Generalized anxiety disorder: diagnosis and treatment. *BMJ* 2012; 345:e7500.
21. Lau AW, Edelstein BA, Larkin KT. Psychophysiological arousal in older adults: a critical review. *Clin Psychol Rev* 2001; 21:609–30.
22. Brantley PJ, Mehan DJ Jr, Ames SC, Jones GN. Minor stressors and generalized anxiety disorders among low income patients attending primary care clinics. *J Nerv Ment Dis* 1999; 187:435–40.
23. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the national comorbidity survey. *Arch Gen Psychiatry* 1994; 51:8–19.
24. Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. *Am J Psychiatry* 2001; 158:1568–78.
25. Molina E, Cervilla J, Rivera M, Torres F, Bellon JA, Moreno B, et al. Polymorphic variation at the serotonin 1-A receptor gene is associated with comorbid depression and generalized anxiety. *Psychiatr Genet* 2011; 21:195–201.
26. Moffitt TE, Caspi A, Harrington H, Milne BJ, Melchior M, Goldberg D, et al. Generalized anxiety disorder and depression: childhood risk factors in a birth cohort followed to age 32. *Psychol Med* 2007; 37:441–52.
27. Ormel J, VonKorff M, Ustun TB, Pini S, Korten A, Oldehinkel T. Common mental disorders and disability across cultures. Results from the WHO Collaborative Study on Psychological Problems in General Health Care. *JAMA* 1994; 272:1741–8.
28. Ballenger JC, Davidson JRT, Lecrubier Y, Nutt DJ, Borkovec TD, Rickels K, et al. Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 2001; 62:53–8.
29. Kessler RC, Keller MB, Wittchen H-U. The epidemiology of generalized anxiety disorder. *Psychiatr Clin North Am* 2001; 24:19–39.
30. Rogers MP, Warshaw MG, Goisman RM, Goldenberg I, Rodriguez-Villa F, Mallya G, et al. Comparing primary and secondary generalized anxiety disorder in a long-term naturalistic study of anxiety disorders. *Depress Anxiety* 1999; 10:1–7.
31. Maier W, Gaensicke M, Freyberger HJ, Linz M, Heun R, Lecrubier Y. Generalized anxiety disorder (ICD-10) in primary care from a cross-cultural perspective: a valid diagnostic entity? *Acta Psychiatry Scand* 2000; 101:29–36.
32. Roy-Byrne PP, Katon W. Generalized anxiety disorder in primary care: the precursor/modifier pathway to increased health care utilization. *J Clin Psychiatry* 1997; 58:34–8.
33. Wittchen H-U, Carter RM, Pfister H, Montgomery SA, Kessler RC. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. *Int Clin Psychopharmacol* 2000; 15:319–28.
34. Wittchen H-U, Kessler RC, Beeselo K, Krause P, Hofler M, Hoyer P. Generalized anxiety and depression in primary care: prevalence, recognition and management. *J Clin Psych* 2002; 63:24–34.
35. Nisenson LG, Pepper CM, Schwenk TL, Coyne JC. The nature and prevalence of anxiety disorders in primary care. *Gen Hosp Psychiatry* 1998; 20:21–8.
36. Fricchione G. Generalized anxiety disorder. *N Engl J Med* 2004; 351(7):675–82.
37. Pollack MH, Smoller JW, Lee DK. Approach to the anxious patient. In: Stern TA, Herman JB, Slavin PL, editors. *The MGH guide to psychiatry in primary care*. New York, NY: McGraw-Hill; 1998. pp 23–37.
38. Goldberg RJ, Posner DA. Anxiety in the medically ill. In: Stoudemire A, Fogel BS, Greenberg DB, editors. *The psychiatric care of the medical patient*. New York, NY: Oxford University Press; 2000. pp 165–80.
39. Stein D. Comorbidity in generalised anxiety disorder: impact and implications. *J Clin Psychiatry* 2001; 62:29–34.
40. Olfson M, Fireman B, Weissman MM, Leon AC, Sheehan DV, Kathol RG, et al. Mental disorders and disability among patients in a primary care group practice. *Am J Psychiatry* 1997; 154:1734–40.
41. Bittner A, Goodwin RD, Wittchen HU, Beesdo K, Hofler M, Lieb R. What characteristics of primary anxiety disorders predict subsequent major depressive disorder? *J Clin Psychiatry* 2004; 65:618–26.
42. Power KG, Simpson RJ, Swanson V, Wallace LA, Feistner ATC, Sharp D. A controlled comparison of cognitive-behaviour therapy, diazepam, and placebo, alone and in combination, for the treatment of generalised anxiety disorder. *J Anxiety Disord* 1990; 4:267–92.
43. Schuurmans J, Comijs H, Emmelkamp PM, Gundy CM, Weijnen I, van den Hout M, et al. A randomized, controlled trial of the effectiveness of cognitive-behavioral therapy and sertraline versus a waitlist control group for anxiety disorders in older adults. *Am J Geriatr Psychiatry* 2006; 14:255–63.
44. Mitte K. Meta-analysis of cognitive-behavioral treatments for generalized anxiety disorder: a comparison with pharmacotherapy. *Psychol Bull* 2005; 131:785–95.
45. Hofmann SG, Smits JA. Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *J Clin Psychiatry* 2008; 69:621–32.

Generalized anxiety disorder

46. Hunot V, Churchill R, Silva de Lima M, Teixeira V. Psychological therapies for generalised anxiety disorder. Cochrane Database Syst Rev 2007; 1:CD001848.
47. Butler G, Fennel M, Robson P, Gelder M. Comparison of behavior therapy and cognitive behavior therapy in the treatment of generalized anxiety disorder. J Consult Clin Psychol 1991; 59:167–75.
48. Robinson E, Titov N, Andrews G, McIntyre K, Schwencke G, Solley K. Internet treatment for generalized anxiety disorder: a randomized controlled trial comparing clinician vs. technician assistance. PLoS One 2010; 5:e10942.
49. Ost LG, Breitholtz E. Applied relaxation vs. cognitive therapy in the treatment of generalized anxiety disorder. Behav Res Ther 2000; 38:777–90.
50. Arntz A. Cognitive therapy versus applied relaxation as treatment of generalized anxiety disorder. Behav Res Ther 2003; 41:633–46.