



## HIGH PERCEIVED STRESS AND ITS IMPACT ON ANXIETY, DEPRESSION, AND QUALITY OF LIFE IN PATIENTS WITH CHRONIC DISEASE

Nazish Fathima<sup>1\*</sup>, Swathi M<sup>1</sup>, Manjusha S<sup>1</sup>, Isatrin J. Vadakkiniath<sup>1</sup>, Gururaj A<sup>1</sup>, Sinchana Bojamma P. K<sup>2</sup>

<sup>1\*</sup> Assistant Professor, Department of Pharmacy Practice, Bapuji Pharmacy College, Shamanur Road, S S Layout, Davangere- 577004, Karnataka, India.

<sup>1,2</sup> Bapuji Pharmacy College affiliated to Rajiv Gandhi University of Health Sciences, Davangere – 577004, Karnataka, India.

**\*Corresponding Author: Nazish Fathima**

Assistant Professor, Department of Pharmacy Practice, Bapuji Pharmacy College, Shamanur Road, S S Layout, Davangere- 577004, Karnataka, India. **Email ID:** [naazfathima93@gmail.com](mailto:naazfathima93@gmail.com).

Article Received on 21/07/2023

Article Revised on 10/08/2023

Article Accepted on 31/08/2023

### ABSTRACT

**Objective:** This study aimed to assess the prevalence of stress, anxiety, and depression among patients with chronic diseases and explore the relationship between high perceived stress, anxiety, depression, and quality of life in this population. **Methods:** The study involved 323 patients with chronic diseases at a teaching hospital. Demographics were collected using a self-designed questionnaire. Stress, anxiety, and depression were measured using the Perceived Stress Scale (PSS) and Hospital Anxiety and Depression Scale (HADS). Quality of life (QOL) was assessed with the Short Form 12 (SF-12) questionnaire. Pearson correlation and Chi-square tests analyzed the associations and correlations between high perceived stress, anxiety, depression, and quality of life. **Results:** This study found high rates of stress (68.8%), anxiety (51.2%), and depression (58.9%) in patients with chronic diseases. Positive correlations were observed between stress and anxiety (+0.7) and stress and depression (+0.738). A significant association was found among high perceived stress, anxiety, and depression ( $p < 0.001$ ). Moreover, a negative correlation (-0.509, -0.506) was found between stress and quality of life. These findings highlight the role of high perceived stress as a risk factor for anxiety, depression, and lower quality of life in patients with chronic diseases. **Conclusion:** This study highlights high rates of stress, anxiety, and depression in patients with chronic diseases. The correlations suggest that high perceived stress is associated with anxiety, depression, and lower quality of life. Early identification and effective stress management are vital for improving well-being and quality of life in these patients.

**KEYWORDS:** Chronic diseases, Stress, Anxiety, Depression, Quality of life.

### INTRODUCTION

Chronic illnesses are silently spreading throughout the world, affecting populations in all corners of the globe.<sup>[1]</sup> These conditions, as defined by the Centers for Disease Control and Prevention (CDC), persist for a year or more, significantly impair daily activities, and require ongoing medical treatment.<sup>[2]</sup> The U.S. National Center for Health Statistics adds that chronic illnesses are characterized by lasting three months or more, meeting specific criteria.<sup>[3]</sup> Unlike acute illnesses, chronic diseases cannot be cured by medications or vaccinations and do not resolve on their own.<sup>[4]</sup> The World Health Organization (WHO) identifies chronic illnesses as the leading cause of death and disability worldwide.<sup>[5]</sup> Furthermore, they impose an increasingly heavy burden on individuals, families, societies, and global healthcare systems.<sup>[6]</sup>

In 2019, non-communicable illnesses accounted for seven out of the top ten causes of mortality worldwide, making up 80% of these factors and contributing to 44% of all deaths. As a whole, non-communicable diseases

(NCDs) were responsible for 74% of global fatalities in that year.<sup>[7]</sup> It is noteworthy that nearly three-quarters of deaths caused by NCDs occur in Lower Middle-Income Countries (LMIs), which already face challenges in combating prevalent infectious diseases such as HIV/AIDS and tuberculosis. Given the rapid epidemiological transition in many LMIs, the emergence of NCDs as a leading cause of death poses a dual burden on their healthcare systems.<sup>[8]</sup>

In India, a country with a population of 1.34 billion, scientists who prioritize global health closely monitor the disease prevalence. The majority of India's disease burden consists of two seemingly unrelated clusters: cardiovascular disease and diabetes. These conditions are diagnosed in 18% and 27% of the Indian population, respectively. Notably, the prevalence of both diseases is significantly higher in urban areas compared to rural regions. Shockingly, only 19% of rural residents possess health insurance, and more than 10% lack access to essential medications.<sup>[10]</sup>

People living with chronic diseases encounter substantial challenges that affect their physical and emotional well-being. It is widely recognized that people with chronic illnesses are at a higher risk of encountering mental health issues compared to the general population.<sup>[9, 15]</sup> These mental health problems can have far-reaching effects on various aspects of an individual's life, such as their social interactions and psychological state. Common examples of such mental health challenges include stress, anxiety, depression, post-traumatic stress disorders, obsessive-compulsive disorders, among others.<sup>[11]</sup>

Stress, a process that strains the body in response to external factors, can lead to psychological and biological changes, potentially causing illness. Prolonged stress adversely affects the immune, cardiovascular, neuroendocrine, and central nervous systems.<sup>[12]</sup> Untreated chronic stress can result in disabilities like high blood pressure, insomnia, anxiety, and muscle pain, and increase the risk of heart disease, depression, obesity, and other chronic illnesses. Patients with chronic diseases frequently experience disruptions in their psycho-emotional state<sup>[13]</sup>, with anxiety and depression associated with negative social and individual consequences, including higher healthcare costs and increased risk of physical ailments.<sup>[14]</sup> However, intensified stress can exacerbate anxiety and contribute to mood disorders, particularly depression. When stress persists or recurs, it can further deteriorate the situation.<sup>[12]</sup>

As stress, anxiety, and depression become more prevalent among individuals with chronic diseases, it becomes crucial to understand their impact on overall health. Individuals with self-reported chronic conditions such as angina, arthritis, asthma, and diabetes tend to have lower health-related quality of life scores.<sup>[15]</sup> Studies have identified a reciprocal association between quality of life and mental health outcomes, indicating that quality of life can predict mental health outcomes or have a bidirectional impact.<sup>[14]</sup> The social and economic status, along with the life circumstances, of an individual, are influential factors in determining their quality of life. Various factors directly or indirectly relate to an individual's mental health status. Research has demonstrated a significant correlation between anxiety, depression, and their life circumstances.<sup>[13]</sup>

While there is extensive research demonstrating the correlation between mental health disorders and chronic diseases, there is a scarcity of studies exploring the direct relationship between chronic stress and the development of anxiety and depression as well as the relationship between quality of life and chronic stress. Therefore, it is crucial to further investigate this connection and gain a deeper understanding of its implications.

## MATERIALS AND METHODS

### *Study site and participants*

This cross-sectional study was conducted at SS Institute of Medical Sciences and Research Centre, a tertiary care teaching hospital in Davangere, Karnataka. The study spanned from April 2022 to October 2022 and focused on hospitalized patients with chronic diseases. Out of the 386 identified patients, a total of 323 in-patients were included in the study based on the specified inclusion criteria.

Inclusion criteria for the study comprised patients aged 18 years and above, individuals diagnosed with a chronic illness, and those who expressed willingness to participate. Exclusion criteria involved patients with a history of psychological disorders, individuals under the age of 18 years, those who declined to sign the consent form, and participants who later withdrew from the study.

### *Data collection and study procedure*

The sample size for the study was initially determined using Cochran's formula:  $S = (z_{1-\alpha/2})^2 pq/e^2$ . In this formula, Z represents 1.96 (corresponding to a 95% confidence interval), d represents the absolute error or precision (set at 10%), and p represents the expected proportion in the population based on previous research. Considering a worst-case scenario derived from prior studies, it was assumed that 50% of hospitalized patients might experience anxiety or depression.<sup>[16]</sup>

A questionnaire, developed in both English and Kannada (the primary language of the Karnataka population), was created for the study. Patients who provided written informed consent to participate, completed the questionnaire in a face-to-face setting. On average, it took approximately 20-30 minutes to finish the questionnaire. The questionnaire collected sociodemographic information such as gender, age, marital status, educational level, employment status, income, primary caretakers, social habits, and lifestyle from the participants.

To assess the levels of stress, anxiety, and depression, the study employed the Perceived Stress Scale (PSS) and the Hospital Anxiety and Depression Scale (HADS).

1. **Stress Assessment:** To assess stress levels, a standardized and validated Hindi version of the Perceived Stress Scale (PSS-10)<sup>[17]</sup> was initially used. This version was later translated into the native language (Kannada) and underwent validation by specialists in psychiatry and general medicine. Participants rated the unexpectedness, manageability, and overwhelming nature of their lives over the previous month on a 5-point Likert scale (0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, 4 = very often). The PSS score was calculated as follows:

- For the four positively worded items (items 4, 5, 7, and 8), the scores were reversed as follows: 0 = 4, 1 = 3, 2 = 2, 3 = 1, and 4 = 0.
  - The total score was computed by summing all the item scores.
  - Individual PSS scores could range from 0 to 40, with higher scores indicating higher perceived stress. Scores falling between 0-13 were categorized as low stress, 14-26 as moderate stress, and 27-40 as high perceived stress.
2. Anxiety and Depression Assessment: For assessing anxiety and depression, the Hospital Anxiety and Depression Scale (HADS) developed by Zigmond and Snaith in 1983<sup>[18]</sup> was used. The scale consists of seven questions for each subscale. Total depression and anxiety scores were calculated by summing the responses to the seven questions in each category. Participants were classified as follows.
    - Normal depression or anxiety: Scores ranging from 0 to 7.
    - Borderline depression or anxiety: Scores ranging from 8 to 10.
    - Excessive depression or anxiety: Scores ranging from 11 to 21.
  3. To evaluate the quality of life (QOL) among patients with chronic diseases, the Short Form 12 (SF-12) scale<sup>[19]</sup> was employed. The SF-12 questionnaire comprises 12 questions that pertain to the patient's physical and mental well-being. Six of these questions assess general physical health, yielding a Physical Component Summary (PCS) score, while the remaining six questions assess general mental health, resulting in a Mental Component Summary (MCS) score. The maximum possible score for PCS is 56, while for MCS it is 60. A higher SF-12 score indicates a better health status.

#### Ethical approval

1. Ethical Approval Statement: The study received approval from the Institutional Ethics Committee on Human Subjects Research at Bapuji Pharmacy

College. The reference number for the approval is BPC/IEC/76/2021-2022, dated February 21st, 2022. Subject confidentiality was strictly maintained throughout the entire data collection process and beyond.

2. Informed Consent Statement: Prior to participation in the study, informed consent was obtained from each individual participant included in the research.

#### Statistical analysis

The data collected in this study were entered into a Microsoft Excel spreadsheet and subsequently coded. Analysis of the coded data was performed using SPSS software version 20. Pearson correlation analysis was employed to investigate the correlations between stress and variables such as anxiety, depression, quality of life (mental component score and physical component score), with statistical significance set at a p-value of <0.05. Furthermore, the association between dependent variables such as stress, anxiety, and depression were evaluated using the chi-square test, with statistical significance determined at a p-value of <0.05.

#### RESULTS

A total of 323 participants with chronic disease were included in this study. The chronic diseases included here are cardiovascular diseases, metabolic diseases, respiratory diseases, cancer, kidney disease, liver diseases and degenerative disorders.

#### Demographic characteristics of the participants

**Table 1** shows demographic details of the study participants were the majority of participants fell within the age range of 18 to 64 years (71.5%), and 56.3% were male. The study population predominantly comprised married individuals, with 78.6% reporting being married and taken care of by their spouses. Around one-quarter of the participants were illiterate (31.3%), and 52.9% were unemployed. Most participants had a monthly income of less than 5000/- Rupees. In terms of lifestyle, 10.5% of participants had a sedentary lifestyle, while 34.7% had a smoking habit.

**Table 1: Demographic characteristics of the participants.**

Variable	N (%)
<b>Age</b>	
18 - 64	231 (71.5)
65 and more	92 (28.5)
<b>Gender</b>	
Male	182 (56.3)
Female	141 (43.6)
<b>Educational status</b>	
Illiterate	101 (31.3)
Primary	122 (37.8)
Secondary	66 (20.4)
University	34 (10.5)
<b>Marital status</b>	
Widowed	63 (19.5)
Married	254 (78.6)

Single	6 (1.8)
<b>Employment status</b>	
Employed	152 (47.1)
Unemployed	171 (52.9)
<b>Monthly income</b>	
< 5,000/- Rupees	203 (62.8)
> 5,000/- Rupees	120 (37.2)
<b>Life style (Daily activity)</b>	
Sedentary	34 (10.5)
< 1 hour	82 (25.4)
1 hour	78 (24.1)
> 1 hour	129 (39.9)
<b>Social habits</b>	
Nil	188 (58.2)
Smoking	112 (34.7)
Alcoholic	14 (4.3)
Chewing tobacco	9 (2.8)
N frequency, % percentage	

The Perceived Stress Scale (PSS) were used to find the stress levels among all the participants, from which 68.8% participants were found to have high perceived stress, 22% were having moderate stress and 9.2% were having low stress.

The Hospital anxiety and depression scale (HADS) were used to find the anxiety and depression levels in the total subjects. According to the scale, 51.2% participants were having abnormal anxiety levels, 32.6% were having borderline anxiety levels and 16.2% were having normal anxiety levels. Likewise, 58.9% participants were found

to have abnormal depression levels, 22.3% were having borderline depression levels and 18.8% were having normal depression levels.

#### **Correlation of Stress with Anxiety and Depression**

The correlation coefficient +0.7, and +0.738 is significant since the *p-value* is less than 0.001. There is significant positive correlation between stress and anxiety and stress and depression. ie, the anxiety and depression are positive along with an increase in stress. The following **Table 2** interpreting the relation.

**Table 2: Correlation of Stress with Anxiety and Depression.**

Variables	n	Pearson Correlation	Significance ( <i>p-value</i> )
Stress and Anxiety	323	+ 0.7	< 0.001*
Stress and Depression	323	+ 0.738	< 0.001*
n frequency			
*P-value <0.05, considered as statistically significant			

#### **Association between dependent variables using Chi-square test**

**Table 3** interprets that there is significance association between stress, anxiety and depression (*p*<0.001\*). We observe that majority of the patients having low stress (90%, 93.3%) are having anxiety and depression level

normal. Also, majority of the patients in the high perceived stress (64.9%, 77.9%) have their anxiety and depression level abnormal. From this, we can conclude that high perceived stress is a potential risk factor for the development of anxiety and depression in patients with chronic diseases.

**Table 3: Association of Stress with Anxiety and Depression.**

		Level of Stress						$\chi^2$	df	<i>p-value</i>
		Low stress		Moderate stress		High perceived stress				
		f	%	f	%	f	%			
Level of Anxiety	Normal	27	90.0%	23	32.4%	3	1.4%	176.21	4	< 0.001*
	Borderline abnormal	3	10.0%	27	38.0%	75	33.8%			
	Abnormal	0	0.0%	21	29.6%	144	64.9%			
Level of depression	Normal	28	93.3%	26	36.6%	7	3.2%	188.85	4	< 0.001*
	Borderline abnormal	2	6.7%	28	39.4%	42	18.9%			

	<b>Abnormal</b>	0	0.0%	17	23.9%	173	77.9%			
f frequency, % Percentage										
$\chi^2$ chi square, df degree of freedom										
*P-value <0.05, considered as statistically significant										

### Quality of life

**Table 4** shows the quality of life (MCS and PCS) of a patient with chronic disease(s). Only 21.9% of the 323 individuals had excellent MCS, while 78.1% had poor

MCS, according to the findings. Similarly, just 4.9% of patients had good PCS, and 95.1% had poor PCS, indicating significant effects on patients' quality of life.

**Table 4: Quality of life of patient with chronic disease(s)**

Quality of life	MCS		PCS	
	n	%	n	%
<b>Good</b>	71	21.9	16	4.9
<b>Poor</b>	252	78.1	307	95.1
<b>Total</b>	323	100	323	100

QOL Quality of life, n frequency, % percentage, MCS mental component score, PCS physical component score

### Correlation between stress and quality of life

The correlation coefficient - 0.509 and - 0.506, is significant since the *p-value* is less than 0.001. There is

significant negative correlation between stress and quality of life (physical, mental). ie, the quality of life is negative along with an increase in stress. The following **Table 5** interpreting the relation.

**Table 5: Correlation between Stress and QOL (PCS and MCS).**

Variables	n	Pearson Correlation	Significance ( <i>p-value</i> )
Stress and QOL (PCS)	323	- 0.509	< 0.001*
Stress and QOL (MCS)	323	- 0.506	< 0.001*

n frequency, QOL Quality of life  
\*P-value <0.05, considered as statistically significant

### CONCLUSION

In conclusion, our study demonstrates a high prevalence of stress, anxiety, and depression among patients with chronic diseases. The significant positive correlations between stress and anxiety, as well as stress and depression, highlight the strong interconnections between these mental health conditions. Importantly, our findings indicate that high perceived stress is a potential risk factor for the development of anxiety and depression in this patient population. Moreover, we observed a negative correlation between stress and quality of life, indicating that increased perceived stress can have detrimental effects on patients' overall well-being and quality of life. These findings underscore the need for targeted interventions focusing on stress management and mental health support for individuals with chronic diseases to improve their overall well-being and enhance their quality of life.

### ACKNOWLEDGEMENT

We would like to extend our heartfelt gratitude to Dr. A. P. Basavarajappa, our principal, for providing us with the opportunity to acquire knowledge and conduct our study at this esteemed institution. We are sincerely thankful to Dr. Ann Elizabeth George, Dr. Sruthi Viswanathan, Dr. Aksa Johnson, and Dr. G L Prabhushankar, our Assistant Professors from the Department of Pharmacy Practice,

for their valuable advice, insightful comments, and unwavering motivation throughout our project. We deeply appreciate the guidance and support of Dr. Vipin Xavier, our statistician, in navigating the statistical approach of the study. Furthermore, we express our sincere gratitude to all the doctors at the SS Institute of Medical Sciences and Research Centre for their invaluable support and guidance throughout the study. Their expertise and dedication have been instrumental in the success of our research.

### Declaration of Conflicting Interests

The authors declare that there is no conflict of interest in the research work.

### Funding

No funding was provided and the research was carried out entirely at the authors' expense.

### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Author contributions:** SM conceptualized the topic, collected data, analyzed, interpreted the data, did literature review, preparation and review of the main

manuscript. MS also contributed in conceptualizing the topic, analyzed, interpreted the data, did literature review, preparation and review of the main manuscript. IJV contributed in literature review, preparation and review of the main manuscript. GA contributed in collecting data. NF took the guidance and reviewed the main draft. SBPK reviewed the main draft.

## REFERENCE

- Harris RE. Epidemiology of chronic disease: global perspectives. Jones & Bartlett Learning, 2019 Apr 15.
- Centers for Disease Control and Prevention. Chronic Diseases [Internet]. Atlanta: Centers for Disease Control and Prevention; [May 14, 2023]. Available from: <https://www.cdc.gov/chronicdisease/index.htm>
- MedicineNet. Definition of Chronic Disease. (2016). Available from: <http://www.medicinenet.com/script/main/art.asp?articlekey=33490>
- Bernell S, Howard SW. Use your words carefully: what is a chronic disease?. *Front. Public Health*, 2016 Aug 2; 4: 159. <https://doi.org/10.3389/fpubh.2016.00159>
- World Health Organization. Chronic diseases [Internet]. Geneva: World Health Organization; [May 14, 2023]. Available from: [http://www.who.int/topics/chronic\\_diseases/en/](http://www.who.int/topics/chronic_diseases/en/)
- Allegrante JP, Wells MT, Peterson JC. Interventions to support behavioral self-management of chronic diseases. *Annu. Rev. Public Health*, 2019 Apr 1; 40: 127. doi: 10.1146/annurev-publhealth-040218-044008
- WHO. WHO reveals leading causes of death and disability worldwide: 2000-2019;
- WHO. Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013– 2020. 2013. Available from: [http://www.who.int/nmh/publications/ncd\\_action\\_plan/en/](http://www.who.int/nmh/publications/ncd_action_plan/en/) Accessed, August 29, 2022.
- Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiat*, 2015; 72(4): 334-341. doi: 10.1001/jamapsychiatry.2014.2502
- Patel SA, Cunningham SA, Tandon N, Narayan KV. Chronic diseases in India—ubiquitous across the socioeconomic spectrum. *Jama Netw Open*, 2019 Apr 5; 2(4): e190404-. DOI: 10.1001/jamanetworkopen.2019.0404
- Monroe SM, Slavich GM. Psychological stressors: overview. *Stress: Concepts, cognition, emotion, and behaviour*, 2016 Jan 1: 109-15. <https://doi.org/10.1016/B978-0-12-800951-2.00013-3>
- Khan S, Khan RA. Chronic stress leads to anxiety and depression. *Ann Psychiatry Ment Health*, 2017 Jan; 5(1): 1091.
- Gerontoukou EI, Michaelidou S, Rekleiti M, Saridi M, Souliotis K. Investigation of anxiety and depression in patients with chronic diseases. *Health Psychol. Res*, 2015 Sep 30; 3(2).doi: 10.4081/hpr.2015.2123.
- Hohls JK, König HH, Quirke E, Hajek A. Anxiety, Depression and Quality of Life—A Systematic Review of Evidence from Longitudinal Observational Studies. *Int J Environ Res Public Health*, 2021 Nov 16; 18(22): 12022. <https://doi.org/10.3390/ijerph182212022>.
- Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *LANCET*, 2007 Sep 8; 370(9590): 851-8. [https://doi.org/10.1016/S0140-6736\(07\)61415-9](https://doi.org/10.1016/S0140-6736(07)61415-9).
- Fattouh N, Hallit S, Salameh P, Choueiry G, Kazour F, Hallit R. Prevalence and factors affecting the level of depression, anxiety, and stress in hospitalized patients with a chronic disease. *Perspect Psychiatr Care*, 2019 Mar 2; 55(4): 592-9. DOI: 10.1111/ppc.12369.
- Jaiswal AK, Meshram S, Pandey V, Singh A. Standardization and validation of Hindi version of Perceived Stress Scale in Indian sample. *IJHW*, 2021 Sep 1; 12(3): 386-90. <https://iahrw.org/our-services/journals/indian-journal-of-health-wellbeing/>.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatrica. Scand*. 1983 Jun; 67(6): 361-70. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>.
- Pakpour AH, Nourozi S, Molsted S, Harrison AP, Nourozi K, Fridlund B. Validity and reliability of short form-12 questionnaire in Iranian hemodialysis patients.
- Celano CM, Villegas AC, Albanese AM, Gaggin HK, Huffman JC. Depression and anxiety in heart failure: a review. *Harv. Rev. Psychiatry*, 2018 Jul; 26(4): 175.doi: 10.1097/HRP.000000000000162.
- Davey CG, Lopez-Sola C, Bui M, Hopper JL, Pantelis C, Fontenelle LF, Harrison BJ. The effects of stress–tension on depression and anxiety symptoms: evidence from a novel twin modelling analysis. *Psychol. Med*, 2016 Nov; 46(15): 3213-8.DOI: <https://doi.org/10.1017/S003329171600188>.
- Liu X, Cao H, Zhu H, Zhang H, Niu K, Tang N, et al. Association of chronic diseases with depression, anxiety and stress in Chinese general population: The CHCN-BTH cohort study. *J Affect Disord*, 2021 Mar 1; 282: 1278-87. <https://doi.org/10.1016/j.jad.2021.01.040>.
- Wong WS, Chen PP, Yap J, Mak KH, Tam BK, Fielding R. Chronic pain and psychiatric morbidity: a comparison between patients attending specialist orthopedics clinic and multidisciplinary pain clinic. *Pain Med*, 2011 Feb 1; 12(2): 246-59. <https://doi.org/10.1111/j.1526-4637.2010.01044.x>.
- Scott KM, Bruffaerts R, Tsang A, Ormel J, Alonso J, Angermeyer MC, et al. Depression–anxiety

- relationships with chronic physical conditions: results from the World Mental Health Surveys. *J Affect Disord*, 2007 Nov 1; 103(1-3): 113-20. <https://doi.org/10.1016/j.jad.2007.01.015>.
25. Alkhatami AD, Alamin MA, Alqahtani AM, Alsaeed WY, AlKhatami MA, Al-Dhafaeri AH. Depression and anxiety among hypertensive and diabetic primary health care patients: Could patients' perception of their diseases control be used as a screening tool?. *Saudi Med. J*, 2017 Jun; 38(6): 621. DOI: 10.15537/smj.2017.6.17941.
26. Ingle VK, Pandey I, Singh AR, Pakhare A, Kumar S. Screening of patients with chronic medical disorders in the outpatient department for depression using handheld computers as interface and patient health Questionnaire-9 as a tool. *Int. J. Appl. Basic Med. Res*, 2017 Apr; 7(2): 129. DOI: 10.4103/2229-516X.205809.
27. Zhang Y, Chen Y, Ma L. Depression and cardiovascular disease in elderly: current understanding. *J. Clin. Neurosci*, 2018; 47: 1-5. <https://doi.org/10.1016/j.jocn.2017.09.022>.
28. Read JR, Sharpe L, Modini M, Dear BF. Multimorbidity and depression: a systematic review and meta-analysis. *J Affect Disord*, 2017 Oct 15; 221: 36-46. <https://doi.org/10.1016/j.jad.2017.06.009>.
29. Kohlmann S, Gierk B, Hilbert A, Brähler E, Löwe B. The overlap of somatic, anxious and depressive syndromes: a population-based analysis. *J. Psychosom. Res*, 2016 Nov 1; 90: 51-6. <https://doi.org/10.1016/j.jpsychores.2016.09.004>.
30. Einvik G, Dammen T, Omland T. Depression and cardiovascular disease--is there an association?. *Tidsskr Nor Laegeforen*, 2010 Apr 1; 130(7): 729-32. DOI: 10.4045/tidsskr.08.0361.
31. Alexopoulos GS. Depression in the elderly. *LANCET*, 2005 Jun 4; 365(9475): 1961-70. [https://doi.org/10.1016/S0140-6736\(05\)66665-2](https://doi.org/10.1016/S0140-6736(05)66665-2).
32. Seligman F, Nemeroff CB. The interface of depression and cardiovascular disease: therapeutic implications. *Ann Ny Acad Sci*, 2015 May; 1345(1): 25-35. <https://doi.org/10.1111/nyas.12738>.
33. Wittchen HU, Kessler RC, Pfister H, Höfler M, Lieb RJ. Why do people with anxiety disorders become depressed? A prospective-longitudinal community study. *Acta Psychiatr Scand*, 2000 Dec; 102: 14-23. <https://doi.org/10.1111/j.0065-1591.2000.acp29-03.x>.
34. Matcham F, Norton S, Scott DL, Steer S, Hotopf M. Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: secondary analysis of a randomized controlled trial. *Rheumatology*, 2016 Feb 1; 55(2): 268-78. <https://doi.org/10.1093/rheumatology/kev306>.
35. Ng CG, Mohamed S, See MH, Harun F, Dahlui M, Sulaiman AH, et al. Anxiety, depression, perceived social support and quality of life in Malaysian breast cancer patients: a 1-year prospective study. *Health Qual Life Outcomes*, 2015 Dec; 13(1): 1-9. <https://doi.org/10.1186/s12955-015-0401-7>.
36. Zhang L, Xia Y, Zhang Q, Fu T, Yin R, Guo G, et al. The correlations of socioeconomic status, disease activity, quality of life, and depression/anxiety in Chinese patients with rheumatoid arthritis. *Psychol Health Med*, 2017 Jan 2; 22(1): 28-36. <https://doi.org/10.1080/13548506.2016.1198817>.
37. Dehghan M, Jazinizade M, Malakoutikhah A, Madadimahani A, Iranmanesh MH, Oghabian S, et al. Stress and quality of life of patients with cancer: the mediating role of mindfulness. *J. Oncol*, 2020 Dec 11; 2020. <https://doi.org/10.1155/2020/3289521>.