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Prevalence of anxiety and depressive symptoms and its association with multimorbidity and demographic factors among adults in Karachi, Pakistan

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Prevalence of anxiety and depressive symptoms and its association with multimorbidity and demographic factors among adults in Karachi, Pakistan

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Abstract

Objectives

This study aimed to estimate the prevalence of anxiety and depressive symptoms and its association with multimorbidity and demographic characteristic of adults aged 30 years and above in Karachi, Pakistan.

Design

Analytical Cross-sectional

Study Setting and Participants

The study was carried out among a general population aged 30 years and above, residing in the Gulshan-e-Iqbal town of Karachi, Pakistan.

Main Outcome Measures

Presence of anxiety and depressive symptoms assessed via Aga Khan University Anxiety Depression Scale (AKUADS).

Results

The magnitude of anxiety and depressive symptoms was reported as 27.4%. The final multivariate logistic regression revealed that the presence of multimorbidity (AOR=1.34, 95% CI: 1.13, 1.59), the female gender (AOR= 2.41, 95% CI: 1.99, 2.91), illiteracy (AOR=1.59, 95% CI: 1.15, 2.21), the Punjabi ethnicity (AOR=1.69, 95% CI: 1.18, 2.42), and visiting a faith healer (AOR=2.34, 95% CI: 1.86, 2.95) were the significant predictors of anxiety and depressive symptoms.

This study found an alarmingly high burden of anxiety and depressive symptoms among adults aged 30 years and above in Karachi, Pakistan. Multimorbidity, the female gender, ethnicity, illiteracy, and visiting faith healers were predictors of anxiety and depressive symptoms in the country.

Key words

Multimorbidity, anxiety and depression, adults,

Strengths and limitations of this study

- The sample population of this study is representing all union councils of Gulshan Town, Karachi.
- A validated screening tool (AKUADS) was used to assess the presence of anxiety and depressive symptoms.
- This was a cross-sectional survey, so inferences could not be drawn related to causality.
- Our study was based on self-reported information on multimorbidity and anxiety and depression this might have either underestimated or overestimated its prevalence and hence association.

Anxiety and depressive symptoms are major public health issues globally. Depression has been ranked the fourth leading cause of disease burden (1). It is predicted that by the year 2020, it will be the second leading cause of disability and death, after cardio vascular disorders (1-4). The magnitude of anxiety and depression are on the rise in the general population. However, individuals with chronic diseases are at even higher risk of anxiety and depressive symptoms (5-8).

Multimorbidity is the co-occurrence of two or more chronic diseases such as cancer, diabetes, hypertension, stroke, asthma, heart disease, arthritis or osteoporosis within an individual (3, 9, 10). Research found that one in four adults in developed countries have multimorbidity (11, 12). On the other hand, low and middle income countries were the home of 80% of chronic illnesses (13). Another study found that 52% of populations between the ages of 21 to 84 were suffering from multimorbidity (14). Whereas, a study conducted by Garin et al (15) in 2014 found a 67% burden of multimorbidity among elder Spanish females. Reasons for variation in prevalence could be due to the differences in multimorbidity definitions, number of chronic conditions included in studies, diagnostic criteria for medical conditions, and a study's sample size and population characteristics. Literature suggested that the prevalence of multimorbidity rises with age (10, 16) and this burden is reported most commonly in females. Additionally, individuals living in underprivileged areas are at a higher risk of developing multimorbidity (17).

Health care providers often face challenges when dealing with clients who have multimorbidity along with anxiety and depressive symptoms (18, 19) As multimorbidity conditions such as diabetes, hypertension, stroke, asthma, arthritis and osteoporosis have

Anxiety and depression are extremely common and alarmingly underdiagnosed healthcare problems, especially in low income countries. In addition, it is associated with social and self-stigma, which create barrier to mental help seeking behavior of individuals who suffer from mental health issues, which leads to an even greater public health concern. Furthermore, anxiety and depression are specifically reported to be common in individuals with multimorbidity (5, 8). However, the studies reporting these associations are mostly conducted in high income countries. To the best of our knowledge, no such population based study has been reported from Pakistan. In a resource limited setting like Pakistan, under diagnosis of mental illnesses can cause potential delay in the initiation of treatment. Hence, it is of utmost importance that anxiety and depression be screened in adults suffering from multimorbidity in order to reduce the burden of complications and suboptimal adherence to the treatment of multimorbidity conditions. Therefore, scarcity of literature from Pakistan requires quantification of the association between anxiety and depression with multimorbidity within the Pakistani population. Thus, the purpose of this study was to estimate the prevalence of anxiety and depressive symptoms and determine the association with multimorbidity and demographic factors among adults aged 30 years and above in Karachi, Pakistan

Methodology

This study was a part of a larger community based research project titled "The Burden of Multimorbidity, Its Patterns and Consequences on Health and Well-Being: The IMPACT Study". The aim of this cross-sectional study was to estimate the burden of anxiety and depressive symptoms and identify the factors associated with multimorbidity. The present study was conducted in the Gulshan-e-Iqbal town of Karachi, Pakistan. A sample of 3250 participants were recruited by using systematic random sampling. This required sample was achieved by using proportionate estimates of the number of individuals in 13 Union Councils (UCs) in the selected town. A Proportionate allocation method was used in order to allocate appropriate weightage to each UC. Within each UC, blocks of houses were selected with a random start, where every 109th (kth sampling interval) household was selected. Individuals within these households who met eligibility criteria were included in the study.

The Aga Khan University Anxiety Depression Scale (AKUADS) was used to assess anxiety and depressive symptoms of the participants. The cutoff score of the scale was 20. At cutoff score of 20, the AKUADS had a sensitivity of 66% and a specificity of 79% (22, 23). The Urdu version of the tool has been validated in the previous research (22). The value of the reliability coefficient tool in our study's population was 0.93.

The study's proposal was approved by The Institutional Review Board (IRB) of Dow University Health Sciences, reference number: Ref: IRB-554/DUHS/Approval/2015/04. Individuals who provided written informed consent were interviewed. A referral plan for counseling was made for participants who scored 20 and above on the AKUADS scale.

The presence of disease was assessed by a combination of self-reported diagnosis, medication use, and laboratory findings. Self-reported disease was determined by the question: "Have you ever been told by a doctor, nurse, or other health professional that you have hypertension, obesity, dyslipidemia, diabetes, heart diseases (Myocardial Infarction and/or chronic ischemic heart diseases), stroke, migraines, asthma and COPD, anemia, thyroid disease, diseases of bones and joints, dyspepsia/peptic ulcer, hepatitis B and C, chronic kidney diseases including stones, cancer, and/or disability?". The following criteria were used to define chronic diseases such as hypertension, obesity, diabetes, and dyspepsia.

A person was said to be hypertensive if they had a high systolic BP (>140 mm Hg) or a high diastolic BP (>90 mm Hg). A person is said to be obese if they had a calculated BMI \geq 30.0 kg/m². A person was said to be diabetic if his blood glucose levels was \geq 200 mg/dl. A person was said to have dyspepsia if they had four or more symptoms of dyspepsia for at least 6 months, based on the Leeds Dyspepsia Questionnaire (LDQ).

Individuals with 2 or more chronic diseases (excluding anxiety and depression) were labeled as having 'multimorbidity' and others who reported one or no chronic medical disease were labeled as having 'no multimorbidity'.

Variables were pre-coded and data was entered and analyzed in the SPSS version 19.0. Descriptive statistics were calculated in the form of frequencies and percentages for categorical variables. Descriptive statistics were calculated in order to estimate the prevalence of anxiety and depressive symptoms. Univariate and multivariate binary logistics regressions were used to assess the associations between anxiety and depressive symptoms and multimorbidity and odd ratios and their 95% confidence intervals were also calculated. The multivariate model was

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adjusted for all variables included in the univariate analysis, and we used significant cutoff as p-value \leq 0.05. This manuscript has followed STROBE cross sectional reporting guidelines (24).

Patient and public involvement

Patients and public were involved in the study and the findings of the research were disseminated using public health awareness programs in the union councils and through direct communication with the study participants.

Results

A total of 3250 participants were interviewed. However, we analyzed our data using information from 2867 study participants. 383 participants were excluded due to missing information on the variables: anxiety & depression symptoms (n=06), presence of multimorbidity (n=09), respondent age (n=06), gender (n=08), education (n=48), income (n=81), occupation (n=72), marital status (n=05), number of children (n=67), ethnicity (n=09), home status (n=14), smoking status (n=66), and visiting faith healer (n=93).

Out of 2867 study participants, 27.4% (n=786) of the participants had anxiety and depressive symptoms. Whereas, 50.2 % (n=1440) of these individuals had reported multimorbidity. In our study, there was an almost equal ratio of male 51.5 % (n=1477) to female 48.5% (n=1390). Regarding education level of the participants, 14% (n=404) had no formal education, 38.3% (n=1098) had higher education, and 20.4% (n=585) had postgraduate education. Regarding monthly household income of participants, 22.3% (n=638) reported their monthly household income to be less than 16,000 rupees and 18.2% (n=523) reported their monthly income to be more than 55,000 rupees. Majority of participants (42% (n=1205)) had professional jobs, 14% (n=389) were labor, 17% (n=484) participants were unemployed. The socio-demographic and other characteristics of the participants are shown in Table 1.

Participants with multimorbidity had higher rate of anxiety and depression symptoms, as compared to participants without multimorbidity (30.7% v/s 24.1%). Females were shown to have higher symptoms of anxiety and depression, as compared to males (36.9% v/s 18.5%). Uneducated groups were more anxious & depressed (39.9%) as compared to other education leveled groups (Primary 29.3%, Secondary 28.1%, Higher/graduate 23.3%, and Post-graduate 25.3%). The participants who had 1-2 children were less anxious & depressed (23.3%), while

those who had no children had higher levels of anxiety & depressive symptoms (30.7%). Among the different linguistic groups, Punjabi and other ethnicities had predominantly higher symptoms of anxiety and depression (32.1%), as compared to the Sindhi ethnicity (20.4%). There was a negative association with smoking and anxiety & depressive symptoms, where smokers were less depressed than nonsmokers (24.1% v/s 28.2%). The participants who used to visit faith healers were more anxious & depressed than non-visiting participants (44.4% v/s 24.4%) (Table 2).

Participants who had multimorbidity had a 34% increased likelihood of being anxious and depressed (AOR=1.34, 95% CI: 1.13, 1.59) as compared to those who reported no multimorbidity. Females were 2.41 times more likely to have anxiety and depressive symptoms as compared to male participants (AOR= 2.41, 95% CI: 1.99, 2.91). The odds of having anxiety and depressive symptoms were 59% higher among participants who had no formal education (AOR=1.59, 95% CI: 1.15, 2.21), as compared to participants who had postgraduate education. Participants who had 1 to 2 children were 32% less likely (AOR=0.68, 95% CI: 0.55, 0.83), and who had 3 and above children were 25% less likely to had anxiety and depressive symptoms (AOR=0.75, 95% CI: 0.59, 0.94) as compared to participants who had no children.

Subjects belonging to the Punjabi ethnicity (AOR=1.69, 95% CI: 1.18, 2.42), spoke Urdu (AOR=1.36, 95% CL: 1.01, 1.81), and participants belonging to other ethnic groups (AOR=1.60, 95% CL: 1.10, 2.24) were more likely to have anxiety and depressive symptoms as compared to Sindhi subjects. In addition, subjects who were visiting a faith healer were 2.34 times more likely (AOR=2.34, 95% CI: 1.86, 2.95) to exhibit anxiety and depressive symptoms as compared to participants who did not visit a faith healer (Table 3).

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This study showed that nearly one fourth of the adult population in Karachi have symptoms of anxiety and depression. This study illustrated that presence of multimorbidity, the female gender, having no children, lower level of education, and visiting a faith healer were significantly associated with higher levels of anxiety and depressive symptoms.

In the present study, an overall prevalence of anxiety and depressive symptoms was 27.4%. The prevalence of anxiety and depression was previously reported to be around 10% and 44% in developed and developing countries, respectively (25, 26). Islam et al in their study, conducted in 2003 (27), found a 28% prevalence of depression among the Bangladesh population. In the United States, the prevalence of anxiety and depression was reported to be 16.2% (28). Papadopoulos et al. (29) reported that the prevalence of depression in Greece was 27%. Whereas, in India, the prevalence of depression was found to be 28% (30). However, in Pakistan, the prevalence of depression and anxiety found to be around 30 to 50 %. (25, 26, 31, 32). A plausible reason of the difference in prevalence of anxiety and depression could be inclusion criteria, sample sizes, recruitment methods, various screening tools, as well as different cutoff points that were employed in these diverse studies (33).

In the past decade, several research studies have established a strong relationship between anxiety & depression and multimorbidity (3, 6, 8, 34). Over all, a positive association was found between the presence of multimorbidity and anxiety and depressive symptoms in our study. Our findings were in concurrence with previous studies, showing a significant association between anxiety and depression and multimorbidity.(3, 8, 35-38). A probable reason could be that mental illness is linked with an unhealthy habits such as the use of smoking, poor self-care, lack of physical activities, and poor medication compliance (36, 39).

In the present study, anxiety and depressive symptoms were found to be strongly associated with females. The prevalence of anxiety and depressive symptoms were found to be 2.5 times higher in females, rather than males. Likewise, previous studies have also revealed a positive association between anxiety, depression, and gender. A research conducted by Mirza and Jenkin (31) found that the prevalence of anxiety and depressive symptoms were 29-66% among females as compared to males, which was 10-33%. A feasible reason for higher prevalence of anxiety and depression among women could be due to biological factors, socioeconomical disadvantages, deprivation of social status, maladaptive coping styles, different mental help seeking behaviors, and lack of a support system for females in our country (40).

The current study also found illiteracy as one of the potential risk factors among participants. Similarly, previous studies found a strong association between low levels of education and anxiety and depressive symptoms (41, 42). A plausible reason could be that education in facilitating adaptive coping skills to deal with distress situation and improving self-confidence, self-efficacy, social skills building and sense of control over environment (43).

In our study, participants who had children were less likely to develop anxiety and depressive symptoms. In contrast, other studies found that having more children is a risk factor for anxiety and depression among women (41, 44). The plausible reason could be that parents tend to positively engage and bind to their children's lives by giving continuous love, time, support and commitment, which can all be coping strategies against distress.

Our study also revealed that ethnicity of a participant is linked with anxiety and depressive symptoms. Subjects who were Punjabi and spoke Urdu were more likely to have anxiety and depressive symptoms. Consistent findings were reported by former studies that

A notable finding of our study was that visiting a faith healer was positively associated with anxiety and depression among both genders. In our culture, distressed individuals seek help from traditional healers or faith healers prior to visiting a doctor or psychiatrist for their illness. The plausible reasons could be because of the stigma that is attached to utilizing mental health services (44, 48). Research has shown that only one to two psychiatrists are available to serve the one million population of Pakistan (49). Furthermore, shortage of mental help resources is one of the hindering factors linked with anxiety and depression in this country. Our result is consistent with a past study, where it was reported that sixteen percent of the Pakistani population first approach to faith healer for their illness (50).

Strengths and Limitations

This is the first research that determined an association of anxiety and depressive symptoms with multimorbidity among the population in Karachi, Pakistan. Inferences could not be determined about the causality of the relationship due to cross-sectional nature of study. Potential risk factors like, family history of psychiatric disorders, marital dissatisfaction, domestic violence, maladaptive coping, current life stressors, and death of a love one that could not be addressed in the current study. This study was based on self-reported information on multimorbidity and anxiety and depression. The reliance on self-reported information might have either underestimated or overestimated its prevalence and hence association.

Conclusion

Our research recognized that almost one quarter of the population had anxiety and depressive symptoms. Among females, anxiety and depressive symptoms are twice as common, as compared to males. Early prevention and screenings are key measures to prevent the rising burden of mental disorders when dealing with chronic physical conditions. In order for this to happen, health care professionals need to be trained in the multidisciplinary handling of physical and mental illnesses.. In addition, general physicians should be well equipped with the knowledge of signs and symptoms of anxiety and depressive symptoms.

Author Contributions

SF conceived the research question, conducted all the literature reviews, data collection, and management, and manuscript drafting and reviewing. MTK reviewed the manuscript and helped in data analysis. SZ helped in the analysis and preparation of tables. KS supervised the research project and conducted the final editing and review of the manuscript. The final version of manuscript was seen and approved by all contributors.

Conflicts of Interest

None

Data Statement

Data is available on request

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References

- 1. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic disease and decrements in health: Evidence from the World Health Surveys. Lancet. 2007;369:851-8.
- 2. Mathers C, Fat DM, Boerma JT. The global burden of disease: 2004 update: World Health Organization; 2008.
- 3. O'Connor K, Vizcaino M, Ibarra JM, Balcazar H, Perez E, Flores L, et al. Multimorbidity in a Mexican Community: Secondary Analysis of Chronic Illness and Depression Outcomes. International journal of nursing (New York, NY). 2015;2(1):35.
- 4. WHO. Depression and other common mental disorders: global health estimates. 2017.
- 5. Deschênes SS, Burns RJ, Schmitz N. Associations between depression, chronic physical health conditions, and disability in a community sample: A focus on the persistence of depression. Journal of affective disorders. 2015;179:6-13.
- 6. Winkler P, Horáček J, Weissová A, Šustr M, Brunovský M. Physical Comorbidities in Depression Co-Occurring with Anxiety: A Cross Sectional Study in the Czech Primary Care System. International journal of environmental research and public health. 2015;12(12):15728-38.
- 7. Levinson D, Karger CJ, Haklai Z. Chronic physical conditions and use of health services among persons with mental disorders—results from the Israel National Health Survey. General hospital psychiatry. 2008;30(3):226-32.
- 8. Gunn JM, Ayton DR, Densley K, Pallant JF, Chondros P, Herrman HE, et al. The association between chronic illness, multimorbidity and depressive symptoms in an Australian primary care cohort. Social psychiatry and psychiatric epidemiology. 2012;47(2):175-84.
- 9. Khanam MA, Streatfield PK, Kabir ZN, Qiu C, Cornelius C, Wahlin Å. Prevalence and patterns of multimorbidity among elderly people in rural Bangladesh: a cross-sectional study. Journal of health, population, and nutrition. 2011;29(4):406.
- 10. Liddy C, Blazkho V, Mill K. Challenges of self-management when living with multiple chronic conditions Systematic review of the qualitative literature. Canadian Family Physician. 2014;60(12):1123-33.
- 11. Ahmadi B, Alimohammadian M, Yaseri M, Majidi A, Boreiri M, Islami F, et al. Multimorbidity: Epidemiology and Risk Factors in the Golestan Cohort Study, Iran: A Cross-Sectional Analysis. Medicine. 2016;95(7):e2756.
- 12. Alaba O, Chola L. The social determinants of multimorbidity in South Africa. Int J Equity Health. 2013;12(1):1-10.
- 13. Chatterji S, Byles J, Cutler D, Seeman T, Verdes E. Health, functioning, and disability in older adults—present status and future implications. The Lancet. 2015;385(9967):563-75.
- 14. Aarts S, van den Akker M, Bosma H, Tan F, Verhey F, Metsemakers J, et al. The effect of multimorbidity on health related functioning: Temporary or persistent? Results from a longitudinal cohort study. Journal of psychosomatic research. 2012;73(3):211-7.
- 15. Garin N, Olaya B, Perales J, Moneta MV, Miret M, Ayuso-Mateos JL, et al. Multimorbidity patterns in a national representative sample of the Spanish adult population. PloS one. 2014;9(1).
- 16. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Ageing research reviews. 2011;10(4):430-9.
- 17. Orueta JF, Nuño-Solinís R, García-Alvarez A, Alonso-Morán E. Prevalence of multimorbidity according to the deprivation level among the elderly in the Basque Country. BMC public health. 2013;13(1):918.

19. Naqvi H, Khan MM. Depression in primary care: difficulties and paradoxes. JPMA 2005;55(9):393.

- 20. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. The European journal of general practice. 2008;14(sup1):28-32.
- 21. Simon GE, VonKorff M, Barlow W. Health care costs of primary care patients with recognized depression. Archives of general psychiatry. 1995;52(10):850-6.
- 22. Ali BS. Validation of an indigenous screening questionnaire for anxiety and depression in an urban squatter settlement of Karachi. J Coll Physicians Surg Pak. 1998;8:207-11.
- 23. Ali BS, Reza H. Development of an indigenous screening instrument in Pakistan: the Aga Khan University Anxiety and Depression Scale. JPMA 1998;48:261-5.
- 24. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS medicine. 2007;4(10):e296.
- 25. Luni FK, Ansari B, Jawad A, Dawson A, Baig SM. Prevalence of depression and anxiety in a village in Sindh. J Ayub Med Coll Abbottabad. 2009;21(2):68-72.
- 26. Muhammad Gadit AA, Mugford G. Prevalence of depression among households in three capital cities of Pakistan: need to revise the mental health policy. Plos one. 2007;2(2):e209.
- 27. Islam MM, Ali M, Ferroni P, Underwood P, Alam MF. Prevalence of psychiatric disorders in an urban community in Bangladesh. General hospital psychiatry. 2003;25(5):353-7.
- 28. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003;289(23):3095-105.
- 29. Papadopoulos F, Petridou E, Argyropoulou S, Kontaxakis V, Dessypris N, Anastasiou A, et al. Prevalence and correlates of depression in late life: a population based study from a rural Greek town. Int J Geriatr Psychiatry. 2005;20(4):350-7.
- 30. Patel V, Prince M. Ageing and mental health in a developing country: who cares? Qualitative studies from Goa, India. Psychological Medicine. 2001;31(01):29-38.
- 31. Mirza I, Jenkins R. Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review. Bmj. 2004;328(7443):794.
- 32. Ali B, Amanullah S. Prevalence of anxiety and depression in an urban squatter settlement of Karachi. JCPSP, Journal of the College of Physicians and Surgeons-Pakistan. 2000;10(1):4-6.
- 33. Taylor AW, Price K, Gill TK, Adams R, Pilkington R, Carrangis N, et al. Multimorbidity-not just an older person's issue. Results from an Australian biomedical study. BMC public health. 2010;10(1):1.
- 34. Smith DJ, McLean G, Martin D, Langan MJ, Guthrie B, Gunn J, et al. Depression and multimorbidity: a cross-sectional study of 1,751,841 patients in primary care. The Journal of clinical psychiatry. 2014;75(11):1202-8.
- 35. Patten SB. Long-term medical conditions and major depression in a Canadian population study at waves 1 and 2. Journal of affective disorders. 2001;63(1):35-41.
- 36. Patten SB. An analysis of data from two general health surveys found that increased incidence and duration contributed to elevated prevalence of major depression in persons with chronic medical conditions. Journal of clinical epidemiology. 2005;58(2):184-9.
- 37. Patten SB, Wang JL, Williams JV, Currie S. Descriptive epidemiology of major depression in Canada. Canadian journal of psychiatry. 2006;51(2):84.

- 39. Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. Biological psychiatry. 2003;54(3):216-26.
- 40. Zahidie A, Jamali T. An overview of the predictors of depression among adult Pakistani women. Journal of the College of Physicians and Surgeons Pakistan. 2013;23(8):574.
- 41. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. Psychological medicine. 2000;30(02):395-402.
- 42. Lovisi GM, Lopez J, Coutinho ESF, Patel V. Poverty, violence and depression during pregnancy: a survey of mothers attending a public hospital in Brazil. Psychological Medicine. 2005;35(10):1485-92.
- 43. Harpham T. Urbanization and mental health in developing countries: a research role for social scientists, public health professionals and social psychiatrists. Social science & medicine. 1994;39(2):233-45.
- 44. Nisar N, Billoo N, Gadit A. Prevalence of depression and the associated risks factors among adult women in a fishing community. JPMA. 2004;54(10):519-25.
- 45. Riolo SA, Nguyen TA, Greden JF, King CA. Prevalence of depression by race/ethnicity: findings from the National Health and Nutrition Examination Survey III. American Journal of Public Health. 2005;95(6):998-1000.
- 46. Costello DM, Swendsen J, Rose JS, Dierker LC. Risk and protective factors associated with trajectories of depressed mood from adolescence to early adulthood. Journal of consulting and clinical psychology. 2008;76(2):173.
- 47. Lankarani MM, Assari S. Association between number of comorbid medical conditions and depression among individuals with diabetes; race and ethnic variations. Journal of Diabetes & Metabolic Disorders. 2015;14(1):1.
- 48. Mishra N, Nagpal SS, Chadda RK, Sood M. Help-seeking behavior of patients with mental health problems visiting a tertiary care center in north India. Indian journal of psychiatry. 2011;53(3):234.
- 49. Khalily MT. Mental health problems in Pakistani society as a consequence of violence and trauma: a case for better integration of care. International journal of integrated care. 2011;11(4).
- 50. Mubbashar M, Saeed K. Development of mental health services in Pakistan. Eastern Mediterranean health journal. 2001;7:392-6.

Table 1: Socio-demographic and other characteristics of participants (n=2867)

of participants (n=2867)	
Characteristics	n (%)
Anxiety and depressive symptoms	S
No	2081 (72.6)
Yes	786 (27.4)
Presence of multimorbidity	
No	1427 (49.8)
Yes	1440 (50.2)
Age	
30-39 years	1062 (37.0)
40-49 years	816 (28.5)
50-59 years	570 (19.9)
60-69 years	293 (10.2)
≥70 years	126 (4.4)
Gender	
Male	1477 (51.5)
Female	1390 (48.5)
Education	
No education	404 (14.1)
Primary	133 (4.6)
Secondary	647 (22.6)
Higher/Graduation	1098 (38.3)
Post-graduate	585 (20.4)
Income	
<16,000	638 (22.3)
16,001-24,999	426 (14.9)
25,000-39,999	636 (22.2)
40,000-54,999	644 (22.5)
>55,000	523 (18.2)
Occupation	- ()
Unemployed	484 (16.9)
Unskilled worker	243 (8.5)
Skilled worker	250 (8.7)
Labor work	389 (13.6)
Non-manual work	296 (10.3)
Professional office job	1205 (42)
Marital status	1200 (12)
Never Married	272 (9.5)
Currently Married	2437 (85.0)
Widowed/Separated/Divorced	158 (5.5)
"Tao "Tod, Separated, Divorced	130 (3.3)

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3 and above children 643 (22.4)

Ethnicity

 Sindhi
 402 (14.0)

 Punjabi
 318 (11.1)

 Balochi
 94 (3.3)

 Pashtu
 176 (6.1)

 Urdu
 1534 (53.5)

 Others
 343 (12.0)

Home Status

Own 1595 (55.6) Rent 1155 (40.3) Other Arrangement 117 (4.1)

Smoking Status

No 2323 (81.0) Yes 544 (19.0)

Visiting Faith Healer

No 2471 (86.2) Yes 396 (13.8)

Table2. Association of Baseline Characteristics of Participants with Anxiety and Depressive symptoms (N=2867)

Depressive symptoms (N=286/)	Anxiety and depressive symptoms			
	maiety and depres	p-		
	No (< 20 score)	Yes &D# score)	value	
Characteristics	n (%)	n (%)		
Presence of multimorbidity				
No	1083 (75.9)	344 (24.1)	< 0.001	
Yes	998 (69.3)	442 (30.7)		
Age				
30-39 years	777 (73.2)	285 (26.8)	0.457	
40-49 years	604 (74.0)	212 (26.0)		
50-59 years	401 (70.4)	169 (29.6)		
60-69 years	213 (72.7)	80 (27.3)		
≥70 years	86 (68.3)	40 (31.7)		
Gender				
Male	1204 (81.5)	273 (18.5)	< 0.001	
Female	877 (63.1)	513 (36.9)		
Education				
No education	243 (60.1)	161 (39.9)	< 0.001	
Primary	94 (70.7)	39 (29.3)		
Secondary	465 (71.9)	182 (28.1)		
Higher/Graduation	842 (76.7)	256 (23.3)		
Post-graduate	437 (74.7)	148 (25.3)		
Income				
<16,000	459 (71.9)	179 (28.1)	0.774	
16,001-24,999	302 (70.9)	124 (29.1)		
25,000-39,999	462 (72.6)	174 (27.4)		
40,000-54,999	479 (74.4)	165 (25.6)		
>55,000	379 (72.5)	144 (27.5)		
Occupation				
Unemployed	363 (75.0)	121 (25.0)	0.078	
Unskilled worker	169 (69.5)	74 (30.5)		
Skilled worker	175 (70.0)	75 (30.0)		
Labor work	267 (68.6)	122 (31.4)		
Non-manual work	229 (77.4)	67 (22.6)		
Professional office job	878 (72.9)	327 (27.1)		
Marital status				
Never Married	210 (77.2)	62 (22.8)	0.018	
Currently Married	1769 (72.6)	668 (27.4)		
Widowed/separated/divorced	102 (64.6)	56 (35.4)		
Numbers of Children				
No child	866 (69.3)	384 (30.7)	0.001	

Table 3: Univariate and multivariate analysis of factors associated with anxiety & depressive symptoms among adults (n=2867)

Anxiety and depressive symptoms						
Characteristics	COR	•			050/ CI	D Volus
Presence of multimorbidity	COK	95% CI	P-Value	AOR	95% CI	P-Value
No	1			1		
Yes	1.39	1.18,1.64	< 0.001	1.34	1.13,1.59	0.001
	1.57	1.10,1.04	\0.001	1.34	1.13,1.39	0.001
Age 30-39 years	1			1		
40-49 years	0.95	0.77,1.77	0.677	0.90	0.71,1.12	0.345
50-59 years	1.14	0.92,1.40	0.227	0.98	0.76,1.26	0.898
60-69 years	1.02	0.78,1.40	0.873	0.86	0.62,1.18	0.337
≥70 years	1.26	0.85,1.88	0.243	1.26	0.81,1.97	0.309
Gender		,			,	
Male	1			1		
Female	2.58	2.17,3.05	< 0.001	2.41	1.99,2.91	< 0.001
Education					•	
Post-graduate	1			1		
Higher/Graduation	0.89	0.71,1.13	0.363	0.87	0.68,1.12	0.309
Secondary	1.15	0.89,1.48	0.263	1.09	0.81,1.47	0.542
Primary	1.22	0.81,1.85	0.341	1.21	0.75,1.94	0.429
No education	1.95	1.48,2.57	< 0.001	1.59	1.15,2.21	0.005
Income						
>55,000	1			1		
40,000-54,999	0.91	0.69,1.17	0.462	0.91	0.69,1.21	0.541
25,000-39,999	0.99	0.76,1.28	0.947	0.97	0.72,1.31	0.855
16,001-24,999	1.08	0.81,1.43	0.592	0.96	0.68,1.35	0.829
<16,000	1.02	0.79,1.32	0.843	0.79	0.57,1.09	0.158
Occupation						
Professional office job	1			1		
Non-manual work	0.78	0.58,1.06	0.115	0.84	0.59,1.19	0.333
Labor work	1.22	0.95,1.57	0.108	1.41	1.03,1.95	0.034
Skilled worker	1.15	0.85,1.55	0.357	1.35	0.96,1.91	0.078
Unskilled worker	1.17	0.87,1.59	0.292	1.16	0.80,1.67	0.419
Unemployed	0.85	0.71,1.14	0.369	0.98	0.72,1.32	0.889
Marital status						
Never Married	1			1		
Currently Married	1.27	0.94,1.72	0.104	1.16	0.84,1.61	0.380
Widowed/separated/divorced	1.86	1.20,2.86	0.005	1.17	0.72,1.91	0.518
Numbers of Children	1			1		
no child	1			1		

1-2 children	0.68	0.56,0.83	< 0.001	0.68	0.55,0.83	< 0.001
3 and above children	0.84	0.68,1.04	1.040	0.75	0.59,0.94	0.014
Ethnicity						
Sindhi	1			1		
Punjabi	1.84	1.31,2.58	< 0.001	1.69	1.18,2.42	0.004
Balochi	1.26	0.74,2.14	0.385	1.33	0.76,2.32	0.317
Pashtu	1.68	1.12,2.51	0.012	1.41	0.91,2.16	0.118
Urdu	1.45	1.11,1.89	0.006	1.36	1.01,1.81	0.037
Others	1.84	1.32,2.56	< 0.001	1.60	1.10, 2.24	0.012
Home Status						
Own	1			1		
Rent	0.96	0.81,1.14	0.690	0.96	0.80,1.56	0.593
Other Arrangement	0.70	0.44,1.10	0.125	0.64	0.39,1.02	0.070
Smoking Status						
No	1			1		
Yes	0.80	0.65,1.00	0.053	0.90	0.71,1.14	0.381
Visiting Faith Healer						
No	1			1		
Yes	2.44	1.96,3.03	< 0.001	2.34	1.86,2.95	< 0.001
COR = unadjusted odds ratios, Cl						
AOR = odds ratios adjusted for all	l independen	t variables.				

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Prevalence of anxiety and depressive symptoms and its association with multimorbidity and demographic factors: A community based cross sectional survey

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Abstract

Objectives

This study aimed to estimate the prevalence of anxiety and depressive symptoms and its association with multimorbidity and demographic characteristic of adults aged 30 years and above in Karachi, Pakistan.

Design

Observational cross-sectional study

Study Setting and Participants

The study was carried out among a general population aged 30 years and above, residing in Gulshan-e-Iqbal town of Karachi, Pakistan. The study participants were recruited using the systematic random sampling approach based on inclusion criteria. The data from 2867 participants was analyzed.

Main Outcome Measures

Primary outcome of the study was prevalence of anxiety and depressive symptoms measured via Aga Khan University Anxiety Depression Scale (AKUADS). And the secondary outcome of the study was the association of anxiety and depressive symptoms with multimorbidity as well as socio-demographic characteristics of the participants using binary logistic regression.

Results

Out of 2867 individuals, 27.4% participants reported to have anxiety and depressive symptoms. The multivariate logistic regression model revealed that the presence of multimorbidity

(AOR=1.32, 95% CI: 1.11, 1.57), the female gender (AOR= 2.44, 95% CI: 2.04, 2.92), illiteracy (AOR=1.58, 95% CI: 1.16, 2.16), number of children (AOR=0.75, 95% CI: 0.59,0.93), and visiting a faith healer (AOR=2.31, 95% CI: 1.84, 2.90) were the significant factors associated with anxiety and depressive symptoms.

Conclusion

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y and depressive symptoms .

ation, number of children and visiting faith.

Cey words

Multimorbidity, anxiety and depression, adults, This study revealed a moderately high prevalence of anxiety and depressive symptoms among adults aged 30 years and above in Karachi, Pakistan. The key variables associated with anxiety and depressive symptoms include; multimorbidity, female gender, lower level of

Strengths and limitations of this study

- The study sample was a large, community-based, diverse ethnic and socioeconomic group of the population.
- A validated screening tool (AKUADS) assessed the presence of anxiety and depressive symptoms, which thus, enhanced the internal validity of the research.
- Inferences could not be drawn about causality of association due to the nature of the design.
- The study data was self-reported, hence, the results should be interpreted cautiously.

Introduction

Mental illness, anxiety and depressive symptoms are major public health issues. Globally 14% people suffer from mental illness (1). More than three quarter of these populations were linked with low and middle income countries (2). Moreover, depression has been ranked as the fourth leading cause of disease burden (3). Also, it is predicted that by the year 2020, it will be the second leading cause of disability and death after cardio vascular disorders (3-6). The magnitude of anxiety and depression is on the rise among general population. However, individuals with chronic diseases are at even higher risk of developing anxiety and depressive symptoms (7-10).

Multimorbidity is the co-occurrence of two or more chronic diseases such as cancer, diabetes, hypertension, stroke, asthma, heart disease, arthritis or osteoporosis within an individual (5, 11, 12). Research studies suggest that one in four adults in developed countries have multimorbidity (13, 14). On the other hand, low and middle income countries are the home of 80% of chronic illnesses (15). Another study claimsthat 52% of populations between the ages of 21 and 84 years are suffering from multimorbidity (16). Whereas, a study conducted by Garin et al (17) in 2014 found a 67% burden of multimorbidity among elder Spanish females. Furthermore. developing countries such as Bangladesh has the prevalence of multimorbidity as 53.8% among older adults (11). However, the reported burden of multimorbidity is 22% in India, (18), Among Pakistani population aged 18 years and older, it was previously reported as 4.9% (19). Thus, the prevalence of multimorbidity varies from 4.9% to 67% between various countries (19-21). Reasons for variation in prevalence could be due to differences in multimorbidity definitions, number of chronic conditions included in studies, diagnostic criteria for medical conditions, as well as study's sample size and population characteristics. Literature suggests that the prevalence of multimorbidity increases with age (12, 22), and this burden is reported to be more common in females. Additionally, individuals living in underprivileged areas are at a higher risk of developing multimorbidity (23).

Health care providers often face challenges when dealing with clients who have multimorbidity along with anxiety and depressive symptoms (24, 25). As multimorbidity conditions such as diabetes, hypertension, stroke, asthma, arthritis and osteoporosis have synergetic effect with anxiety and depression, it increases the probability of disabilities among patients (7). The presence of anxiety and depression with multimorbidity leads to increased rates of utilizing health care facilities. This consequently leads to financial health care burdens and poorer health outcomes (2, 13, 26, 27). Individuals with multimorbidity need to deal with multiple treatment recommendations (10). Thus, anxiety and depression with multimorbidity is linked with 50% to 100% of the utilization of health services and cost (28)

Anxiety and depression are extremely common and alarmingly underdiagnosed healthcare problems, especially in low and middle income countries. In addition, it is associated with social and self-stigma, which create barrier to mental help seeking behavior of individuals who suffer from mental health issues that further leads to an even greater public health concern. Furthermore, anxiety and depression are specifically reported to be common in individuals with multimorbidity (7, 10). However, the studies that report these associations are mostly conducted in high income countries. To the best of our knowledge, no such population based study has been reported from Pakistan yet. In a resource limited setting like Pakistan, under diagnosis of mental illnesses can cause potential delay in the initiation of treatment. Hence, it is of utmost importance that anxiety and depression be screened in adults suffering from multimorbidity in order to reduce the burden of complications and suboptimal adherence to the treatment of multimorbidity conditions. Therefore, scarcity of literature from Pakistan requires quantification of the association between

anxiety and depression with multimorbidity within the Pakistani population. It was hypothesized that there is an association between anxiety and depressive symptoms and multimorbidity among Pakistani population. Therefore, the purpose of this study was to estimate the prevalence of anxiety and depressive symptoms, and determine the association with multimorbidity and demographic factors among adults aged 30 years and above in Karachi, Pakistan.



Methodology

This study was a part of a larger community based research project titled "The Burden of Multimorbidity, Its Patterns and Consequences on Health and Well-Being: The IMPACT Study", conducted in 2015-2016.

Study design: Cross-sectional study was conducted to estimate the burden of anxiety and depressive symptoms, and to identify their associated factors.

Study population: The study population comprised of all adults of age 30 years and above, and residents of Gulshan-e-Iqbal town, Karachi, Pakistan. This particular age group was selected for this study as chronic medical conditions are more prevalent among them.

Inclusion criteria: All Participants who were aged 30 years and above and who were the residents of Gulshan-e-Iqbal town, Karachi Pakistan and signed the consent form to take part in the study.

Sample size calculation: For the objective of this study, the sample size was calculated using an online version of Open Epi calculator. The prevalence of anxiety and depression is reported to be 30% to 50% among adults in Pakistan (29, 30). With 2% margin of error and 95% confidence level, the required sample size was 2401 participants. Similarly, for secondary objective (association of anxiety and depressive symptoms with multimorbidity), keeping the confidence interval of 95%, 90% power, 1:1 ratio of non-depressed and depressed individuals with odds ratio of 1.55, and proportion of multimorbidity among non-depressed was taken as 10% (Smith et al., 2014), the required sample size was 2148 individuals. In order to account for missing values, a higher sample size (2401) was chosen. However, we have taken 3250 individuals for data collection.

Sampling Technique: The present study was conducted in Gulshan-e-Iqbal town of Karachi, Pakistan. A sample of 3250 participants was recruited by using systematic random sampling. This required sample was achieved by using proportionate estimates of the number of individuals in 13 Union Councils (UCs) in the selected town. A Proportionate allocation method was used in order to allocate appropriate weightage to each UC. Within each UC, blocks of houses were selected with a random start, where every 109th (kth sampling interval) household was selected. Individuals within these households who met the eligibility criteria were included in the study.

Data Collection: Data were collected from participants by interviewing them with the help of structured questionnaire. The questionnaire was developed after thorough literature review to collect data about socio demographic information (including age, gender, marital status, educational status, employment status, mother tongue, number of family members and information about housing, presence of any chronic disease, and living condition of each participant. Participants were interviewed by trained data collectors, the anthropometric measurements as well as Blood Pressure were measured by trained health professionals mainly included doctors and nurses who were involved in data collection.

Dependent variable: The Aga Khan University Anxiety Depression Scale (AKUADS) was used to assess anxiety and depressive symptoms of the participants. This tool has a total of 25 questions and for each of the questions the participant can choose an answer from Never (scored as 0), Sometime (scored as 1), Often (scored as 2), Always (scored as 3). The cumulative cutoff score of 20 or greater at this scale is used to label anxiety and depression. At cutoff score of 20, the AKUADS had a sensitivity of 66% and a specificity of 79% (31, 32). This study used the Urdu version of the AKUADS which had been validated in a previous research (31). The value of the

reliability coefficient tool in our study's population was 0.93. **Independent Variables**: The presence of disease was assessed by a combination of self-reported diagnosis, medication use, and laboratory findings. Self-reported disease was determined by the question: "Have you ever been told by a doctor, nurse, or other health professional that you have hypertension, dyslipidemia, diabetes, heart diseases (Myocardial Infarction and/or chronic ischemic heart diseases), stroke, migraines, asthma and COPD, anemia, thyroid disease, diseases of bones and joints, dyspepsia/peptic ulcer, hepatitis B and C, chronic kidney diseases including stones, cancer, and/or disability?". The following criteria were used to define chronic diseases such as hypertension, obesity, diabetes, and dyspepsia.

A person was said to be hypertensive if that person had a high systolic BP (>140 mm Hg) or a high diastolic BP (>90 mm Hg). A person is said to be obese if they had a calculated BMI \geq 30.0 kg/m². A person was said to be diabetic if his blood glucose level was \geq 200 mg/dl. A person was considered having dyspepsia if they had four or more symptoms of dyspepsia for at least 6 months, based on the Leeds Dyspepsia Questionnaire (LDQ).

Individuals with 2 or more chronic diseases (excluding anxiety and depression) were labeled as having 'multimorbidity' and others who reported one or no chronic medical disease were considered as having 'no multimorbidity'.

Beside disease related variables, other sociodemographic variables were also measured such as household income, occupation and education. This variable was initially taken as continuous variable such as what is your monthly income (in Pakistani Rupees). Then it was further classified into quintiles i.e. < 16000, 16001-24999, 25000-39999, 40000-54999 and 55000 rupees and above. Occupation of all participants was also assessed as a categorical variable and had following categories such as unemployed, unskilled worker, skilled worker, labor worker, non-manual

worker and professional office job. Data on education were collected as total number of years of full education, which was then categorized into five categories as follows:

- a. No education (0 years or those who never attended school)
- b. Primary (1-5 years)
- c. Secondary (6-10 years)
- d. Higher education (11-14 years)
- e. Postgraduate (≥15 years)

Ethical considerations: The study's proposal was approved by The Institutional Review Board (IRB) of Dow University Health Sciences, reference number: Ref: IRB-554/DUHS/Approval/2015/04. Individuals who provided written informed consent were interviewed. A referral plan for counseling was made for participants who scored 20 and above on the AKUADS scale.

Statistical Analysis: Variables were pre-coded and data was entered and analyzed in the SPSS version 19.0. Descriptive statistics were calculated in the form of frequencies and percentages for categorical variables. Descriptive statistics were calculated in order to estimate the prevalence of anxiety and depressive symptoms. Univariate and multivariate binary logistics regressions were used to assess the associations between anxiety and depressive symptoms and multimorbidity and odd ratios and their 95% confidence intervals were also calculated. The multivariate model was adjusted for only variables with p-values <0.250 in univariate analysis using a step-wise logistic

regression method. This manuscript has followed STROBE cross sectional reporting guidelines (33).

Patient and public involvement: In current study patient and participants were not involved in nent: The data is available on . the research question, study design, outcome measure and recruitment.

Data availability statement: The data is available on request from the corresponding author.

Results

A total of 3250 participants were interviewed. However, the data were analyzed using information from 2867 study participants. Of the total, 383 participants were excluded due to missing information on the variables: anxiety & depression symptoms (n=06), presence of multimorbidity (n=09), respondent age (n=06), gender (n=08), education (n=48), income (n=81), occupation (n=72), marital status (n=05), number of children (n=67), ethnicity (n=09), home status (n=14), smoking status (n=66), and visiting faith healer (n=93).

Out of 2867 study participants, the mean age was 45.5 years (SD±11.7 years). In the study, there was an approximately equal ratio of male 51.5 % (n=1477) to female 48.5% (n=1390). Regarding educational level of the participants, 14% (n=404) had no formal education, 38.3% (n=1098) had higher education, and 20.4% (n=585) had postgraduate education. In addition, 22.3% (n=638) reported their monthly household income to be less than 16,000 rupees while 18.2% (n=523)claimed their monthly income to be more than 55,000 rupees. Majority of participants 42% (n=1205) had professional jobs, 14% (n=389) were labor, and 17% (n=484) participants were unemployed. In our study, participants reported anxiety and depressive symptoms and multimorbidity to be 27.4% (n=786) and 50.2% (n=1440), respectively. The sociodemographic and other characteristics of the participants are shown in Table 1.

Adjusted model revealed that, participants who had multimorbidity had a 32% increased odds of being anxious and depressed (AOR=1.32, 95% CI: 1.11, 1.57) as compared to those who reported no multimorbidity. The odds of having anxiety and depressive symptoms were 2.44 times higher among females as compared to male participants (AOR= 2.44, 95% CI:2.04, 2.92). The odds of having anxiety and depressive symptoms were 58% higher among participants who had no formal education (AOR=1.58, 95% CI: 1.16, 2.16), as compared to participants who had

postgraduate education. The odds of being anxious and depressed were 1.35 times higher among participants who were labor workers as compared to participants who were doing professional office jobs (AOR=1.35, 95% CI: 1.01, 1.79). Study participants who had 1 to 2 children were 32% less likely (AOR=0.68, 95% CI: 0.56, 0.84), and who had more than two children were 25% less likely (AOR=0.75, 95% CI: 0.59, 0.93) to had anxiety and depressive symptoms as compared to participants who had no children. In addition, subjects who were visiting a faith healer were 2.31 times (AOR=2.31, 95% CI: 1.84, 2.9) odds of exhibiting anxiety and depressive symptoms as compared to participants who did not visit a faith healer (Table 2).

Table 3 showed the estimated association of anxiety and depressive symptoms and number of chronic diseases. The anxiety and depressive symptoms were significantly associated with increasing number of chronic diseases. The odds of anxiety and depressive symptoms were highest among individuals with four chronic diseases (AOR=1.92, 95% CI: 1.33, 2.78), and more than four chronic diseases (AOR=2.62, 95% CI: 1.66, 4.13), compared with healthy individuals when adjusted for other variables (Table 3).

Discussion

This study showed that nearly one fourth of the adult population in Karachi have symptoms of anxiety and depression. This study illustrated that presence of multimorbidity, female gender, lower level of education, number of children and visiting a faith healer were significantly associated with anxiety and depressive symptoms.

Current study used a screening tool (AKUADS) to assess the presence of anxiety and depressive symptoms. In the present study, an overall prevalence of anxiety and depressive symptoms was 27.4%. The prevalence of anxiety and depression was previously reported to be around 10% and 44% in developed and developing countries, respectively (34, 35). Islam et al in their study conducted in 2003 (36), found a 28% prevalence of depression among the Bangladesh population. In the United States, the prevalence of anxiety and depression was reported to be 16.2% (37). Papadopoulos et al. (38) reported that the prevalence of depression in Greece was 27%. Whereas, in India, the prevalence of depression was found to be 28% (39). However, in Pakistan, the prevalence of depression and anxiety found to be around 30 to 50 %. (29, 34, 35, 40). A plausible reason of the difference in prevalence of anxiety and depression could be due to the inclusion criteria, sample sizes, recruitment methods, various screening tools, as well as different cutoff points that were employed in these diverse studies (21).

In the past decade, several research studies have established a strong relationship between anxiety and depression and multimorbidity (5, 8, 10, 41). Moving on, our findings were in concurrence with previous studies, showing a significant association between anxiety and depression and multimorbidity.(5, 10, 42-45). A probable reason could be that mental illness is linked with an unhealthy habits such as the use of smoking, poor self-care, lack of physical activities, and poor medication compliance (43, 46).

In the present study, anxiety and depressive symptoms were found to be strongly associated with females. The prevalence of anxiety and depressive symptoms were found to be 2.5 times higher in females, rather than males. Likewise, previous studies have also revealed a positive association between anxiety, depression, and gender. A research conducted by Mirza and Jenkin (40) found that the prevalence of anxiety and depressive symptoms were 29-66% among females as compared to males, which was 10-33%. A plausible reason for higher prevalence of anxiety and depression among women could be due to biological factors, socio-economical disadvantages, deprivation of social status, maladaptive coping styles, and lack of a support system for females in our country (47).

The current study also found illiteracy as one of the potential risk factors among participants. Similarly, previous studies found a strong association between low levels of education and anxiety and depressive symptoms (48, 49). Whereas, among the literate population, education could be one of the reasons that facilitates their adaptive coping skills to deal with distress situation and improving self-confidence, self-efficacy, social skills building and sense of control over environment (50).

In our study, participants who bore more children were less likely to develop anxiety and depressive symptoms. The plausible reason could be that parents tend to positively engage and bind to their children's lives by giving continuous love, time, support and commitment, which can all be coping strategies against distress. In contrast, other studies found that having more children is a risk factor for anxiety and depression among women (48, 51). This could be due to the extra burden of responsibilities that woman has to fulfill in our society; whereas, as per societal norms, males are not expected to take part in household chores and traditional child care.

A notable finding of our study was that visiting a faith healer was positively associated with anxiety and depression among both genders. In our culture, distressed individuals seek help from traditional healers or faith healers prior to visiting a doctor or psychiatrist for their illness. However, a few probable reasons for visiting faith healers could be due to easy accessibility, availability and affordability, cultural beliefs and the predominant stigma attached to the notion of mental illness (51, 52). Moreover, in our culture many people believe that mental illnesses are due to wrongdoings, being possessed, witchcraft and spirit; hence the affected population consults with these faith healers rather than doctors. Our result is consistent with a past study, where it was reported that sixteen percent of the Pakistani population first approach to faith healer for their illness (53). Therefore, there is a dire need to create awareness regarding identification of symptoms of mental illness and to develop proper referral system for essential treatment on early stage of disease to avoid delayed presentation with more advanced disease.

Strengths and Limitations

This is the first research that determined an association of anxiety and depressive symptoms with multimorbidity among the population in Pakistan. Inferences could not be determined about the causality of the relationship due to cross-sectional nature of study. Potential risk factors such as, family history of psychiatric disorders, marital dissatisfaction, domestic violence, maladaptive coping, current life stressors, and death of a loved one that could not be addressed in the current study. This study was based on self-reported information on multimorbidity and anxiety and depression.

Conclusion

This study suggests that almost one quarter of the population had anxiety and depressive symptoms. Among females, anxiety and depressive symptoms are twice as common, as compared to males. Early prevention and screenings are key measures to prevent the rising burden of mental disorders when dealing with chronic physical conditions.

Author Contributions

KS, SF conceived the research question and design of this project. SF conducted all the literature reviews and manuscript drafting and reviewing as well as took part in data collection. MTK and SZ helped in the data analysis, preparation of tables, and reviewed the manuscript. KS supervised the research project and conducted the final editing and review of the manuscript. The final version of manuscript was seen and approved by all contributors.

Conflicts of Interest

None

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References

- 1. Yatham S, Sivathasan S, Yoon R, da Silva TL, Ravindran AV. Depression, anxiety, and post-traumatic stress disorder among youth in low and middle income countries: a review of prevalence and treatment interventions. Asian J Psychiatr. 2018;38:78-91.
- 2. Jordans MJ, Kaufman A, Brenman NF, Adhikari RP, Luitel NP, Tol WA, et al. Suicide in South Asia: a scoping review. BMC psychiatry. 2014;14(1):358.
- 3. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic disease and decrements in health: Evidence from the World Health Surveys. Lancet. 2007;369:851-8.
- 4. Mathers C, Fat DM, Boerma JT. The global burden of disease: 2004 update: World Health Organization; 2008.
- 5. O'Connor K, Vizcaino M, Ibarra JM, Balcazar H, Perez E, Flores L, et al. Multimorbidity in a Mexican Community: Secondary Analysis of Chronic Illness and Depression Outcomes. Int J Nurs. 2015;2(1):35.
- 6. WHO. Depression and other common mental disorders: global health estimates. 2017.
- 7. Deschênes SS, Burns RJ, Schmitz N. Associations between depression, chronic physical health conditions, and disability in a community sample: A focus on the persistence of depression. J Affect Disord. 2015;179:6-13.
- 8. Winkler P, Horáček J, Weissová A, Šustr M, Brunovský M. Physical Comorbidities in Depression Co-Occurring with Anxiety: A Cross Sectional Study in the Czech Primary Care System. Int J Environ Res Public Health. 2015;12(12):15728-38.
- 9. Levinson D, Karger CJ, Haklai Z. Chronic physical conditions and use of health services among persons with mental disorders—results from the Israel National Health Survey. Gen Hosp Psychiatry. 2008;30(3):226-32.
- 10. Gunn JM, Ayton DR, Densley K, Pallant JF, Chondros P, Herrman HE, et al. The association between chronic illness, multimorbidity and depressive symptoms in an Australian primary care cohort. Soc Psychiatry Psychiatr Epidemiol. 2012;47(2):175-84.
- 11. Khanam MA, Streatfield PK, Kabir ZN, Qiu C, Cornelius C, Wahlin Å. Prevalence and patterns of multimorbidity among elderly people in rural Bangladesh: a cross-sectional study. J Health Popul Nutr. 2011;29(4):406.
- 12. Liddy C, Blazkho V, Mill K. Challenges of self-management when living with multiple chronic conditions Systematic review of the qualitative literature. Can Fam Physician. 2014;60(12):1123-33.
- 13. Ahmadi B, Alimohammadian M, Yaseri M, Majidi A, Boreiri M, Islami F, et al. Multimorbidity: Epidemiology and Risk Factors in the Golestan Cohort Study, Iran: A Cross-Sectional Analysis. Medicine. 2016;95(7):e2756.
- 14. Alaba O, Chola L. The social determinants of multimorbidity in South Africa. Int J Equity Health. 2013;12(1):1-10.
- 15. Chatterji S, Byles J, Cutler D, Seeman T, Verdes E. Health, functioning, and disability in older adults—present status and future implications. Lancet. 2015;385(9967):563-75.
- 16. Aarts S, van den Akker M, Bosma H, Tan F, Verhey F, Metsemakers J, et al. The effect of multimorbidity on health related functioning: Temporary or persistent? Results from a longitudinal cohort study. J Psychosom Res. 2012;73(3):211-7.
- 17. Garin N, Olaya B, Perales J, Moneta MV, Miret M, Ayuso-Mateos JL, et al. Multimorbidity patterns in a national representative sample of the Spanish adult population. PloS one. 2014;9(1).
- 18. Akinsulore A, Esimai OA, Afolabi OT, Aloba OO, Mapayi BM. Prevalence and factors associated with depressive symptoms among Yoruba adults in a semi-urban community in South-Western Nigeria. J Behav Health. 2015;4(3):81-6.

- 19. Afshar S, Roderick PJ, Kowal P, Dimitrov BD, Hill AG. Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys. BMC public health. 2015:15(1):1.
- 20. Roberts K, Rao D, Bennett T, Loukine L, Jayaraman G. Prevalence and patterns of chronic disease multimorbidity and associated determinants in Canada. Health Promotion. 2015;35(6):87-94.
- 21. Taylor AW, Price K, Gill TK, Adams R, Pilkington R, Carrangis N, et al. Multimorbidity-not just an older person's issue. Results from an Australian biomedical study. BMC public health. 2010;10(1):1.
- 22. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Ageing Res Rev. 2011;10(4):430-9.
- 23. Orueta JF, Nuño-Solinís R, García-Alvarez A, Alonso-Morán E. Prevalence of multimorbidity according to the deprivation level among the elderly in the Basque Country. BMC public health. 2013;13(1):918.
- 24. Roca M, Gili M, Garcia-Garcia M, Salva J, Vives M, Campayo JG, et al. Prevalence and comorbidity of common mental disorders in primary care. J Affect Disord. 2009;119(1):52-8.
- 25. Naqvi H, Khan MM. Depression in primary care: difficulties and paradoxes. JPMA 2005;55(9):393.
- 26. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. Eur J Gen Pract. 2008;14(sup1):28-32.
- 27. Lockett H, Lai J, Tuason C, Jury A, Fergusson D. Primary healthcare utilisation among adults with mood and anxiety disorders: an analysis of the New Zealand Health Survey. J Prim Health Care. 2018;10(1):68-75.
- 28. Simon GE, VonKorff M, Barlow W. Health care costs of primary care patients with recognized depression. Arch Gen Psychiatry. 1995;52(10):850-6.
- 29. Ali B, Amanullah S. Prevalence of anxiety and depression in an urban squatter settlement of Karachi. J Coll Physicians Surg Pak. 2000;10(1):4-6.
- 30. Waheed A, Hameed K, Khan AM, Syed J, Mirza AI. The burden of anxiety and depression among patients with chronic rheumatologic disorders at a tertiary care hospital clinic in Karachi, Pakistan. JPMA. 2006;56(5):243-7.
- 31. Ali BS. Validation of an indigenous screening questionnaire for anxiety and depression in an urban squatter settlement of Karachi. J Coll Physicians Surg Pak. 1998;8:207-11.
- 32. Ali BS, Reza H. Development of an indigenous screening instrument in Pakistan: the Aga Khan University Anxiety and Depression Scale. JPMA 1998;48:261-5.
- 33. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med. 2007;4(10):e296.
- 34. Luni FK, Ansari B, Jawad A, Dawson A, Baig SM. Prevalence of depression and anxiety in a village in Sindh. J Ayub Med Coll Abbottabad. 2009;21(2):68-72.
- 35. Muhammad Gadit AA, Mugford G. Prevalence of depression among households in three capital cities of Pakistan: need to revise the mental health policy. Plos one. 2007;2(2):e209.
- 36. Islam MM, Ali M, Ferroni P, Underwood P, Alam MF. Prevalence of psychiatric disorders in an urban community in Bangladesh. Gen Hosp Psychiatry. 2003;25(5):353-7.
- 37. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003;289(23):3095-105.
- 38. Papadopoulos F, Petridou E, Argyropoulou S, Kontaxakis V, Dessypris N, Anastasiou A, et al. Prevalence and correlates of depression in late life: a population based study from a rural Greek town. Int J Geriatr Psychiatry. 2005;20(4):350-7.

- 39. Patel V, Prince M. Ageing and mental health in a developing country: who cares? Qualitative studies from Goa, India. Psychol Med. 2001;31(01):29-38.
- 40. Mirza I, Jenkins R. Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review. BMJ. 2004;328(7443):794.
- 41. Smith DJ, McLean G, Martin D, Langan MJ, Guthrie B, Gunn J, et al. Depression and multimorbidity: a cross-sectional study of 1,751,841 patients in primary care. J Clin Psychiatry. 2014;75(11):1202-8.
- 42. Patten SB. Long-term medical conditions and major depression in a Canadian population study at waves 1 and 2. J Affect Disord. 2001;63(1):35-41.
- 43. Patten SB. An analysis of data from two general health surveys found that increased incidence and duration contributed to elevated prevalence of major depression in persons with chronic medical conditions. J Clin Epidemiol. 2005;58(2):184-9.
- 44. Patten SB, Wang JL, Williams JV, Currie S. Descriptive epidemiology of major depression in Canada. Can J Psychiatry. 2006;51(2):84.
- 45. Spangenberg L, Forkmann T, Braehler E, Glaesmer H. The association of depression and multimorbidity in the elderly: implications for the assessment of depression. Psychogeriatrics. 2011;11(4):227-34.
- 46. Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. Biol Psychiatry. 2003;54(3):216-26.
- 47. Zahidie A, Jamali T. An overview of the predictors of depression among adult Pakistani women. J Coll Physicians Surg Pak. 2013;23(8):574.
- 48. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. Psychol Med. 2000;30(02):395-402.
- 49. Lovisi GM, Lopez J, Coutinho ESF, Patel V. Poverty, violence and depression during pregnancy: a survey of mothers attending a public hospital in Brazil. Psychol Med. 2005;35(10):1485-92.
- 50. Harpham T. Urbanization and mental health in developing countries: a research role for social scientists, public health professionals and social psychiatrists. Soc Sci Med. 1994;39(2):233-45.
- 51. Nisar N, Billoo N, Gadit A. Prevalence of depression and the associated risks factors among adult women in a fishing community. JPMA. 2004;54(10):519-25.
- 52. Mishra N, Nagpal SS, Chadda RK, Sood M. Help-seeking behavior of patients with mental health problems visiting a tertiary care center in north India. Indian J Psychiatry. 2011;53(3):234.
- 53. Mubbashar M, Saeed K. Development of mental health services in Pakistan. East Mediterr Health J. 2001;7:392-6.

Table 1: Socio-demographic and other characteristics of participants (n=2867)

Characteristics	n (%)	_
Anxiety and depressive sympton	ıs	_
No	2081 (72.6)	
Yes	786 (27.4)	
Presence of multimorbidity		
No	1427 (49.8)	
Yes	1440 (50.2)	
Age		
30-39 years	1062 (37.0)	
40-49 years	816 (28.5)	
50-59 years	570 (19.9)	
60-69 years	293 (10.2)	
≥70 years	126 (4.4)	
Gender		
Male	1477 (51.5)	
Female	1390 (48.5)	
Education		
No education	404 (14.1)	
Primary	133 (4.6)	
Secondary	647 (22.6)	
Higher/Graduation	1098 (38.3)	
Post-graduate	585 (20.4)	
Income		
<16,000	638 (22.3)	
16,001-24,999	426 (14.9)	
25,000-39,999	636 (22.2)	
40,000-54,999	644 (22.5)	
>55,000	523 (18.2)	
Occupation		
Unemployed	484 (16.9)	
Unskilled worker	243 (8.5)	
Skilled worker	250 (8.7)	
Labor work	389 (13.6)	
Non-manual work	296 (10.3)	
Professional office job	1205 (42)	
Marital status		

Never Married	272 (9.5)
Currently Married	2437 (85.0)
Widowed/Separated/Divorced	158 (5.5)
Numbers of Children	
No child	1250 (43.6)
1-2 children	974 (34.0)
3 and above children	643 (22.4)
Ethnicity	
Sindhi	402 (14.0)
Punjabi	318 (11.1)
Balochi	94 (3.3)
Pashtu	176 (6.1)
Urdu	1534 (53.5)
Others	343 (12.0)
Home Status	
Own	1595 (55.6)
Rent	1155 (40.3)
Other Arrangement	117 (4.1)
Smoking Status	
No	2323 (81.0)
Yes	544 (19.0)
Visiting Faith Healer	
No	2471 (86.2)
Yes	396 (13.8)

Table 2: Univariate and multivariate analysis of factors associated with anxiety & depressive symptoms among adults (n=2867)

		Anxiety and d	lepressive sym	nptoms
Characteristics	COR	95% CI	AOR	95% CI
Presence of multimorbidity				
No	1		1	
Yes	1.39	1.18,1.64	1.32	1.11,1.57
Age				
30-39 years	1		-	
40-49 years	0.95	0.77,1.77	-	
50-59 years	1.14	0.92,1.40	-	
60-69 years	1.02	0.78,1.40	-	
≥70 years	1.26	0.85,1.88	-	
Gender				
Male	1		1	
Female	2.58	2.17,3.05	2.44	2.04,2.92
Education				

	D				
	Post-graduate	1		1	
	Higher/Graduation	0.89	0.71,1.13	0.88	0.69,1.13
	Secondary	1.15	0.89,1.48	1.08	0.81,1.44
	Primary	1.22	0.81,1.85	1.12	0.71,1.78
	No education	1.95	1.48,2.57	1.58	1.16,2.16
Inc	ome				
	>55,000	1		-	
	40,000-54,999	0.91	0.69,1.17	-	
	25,000-39,999	0.99	0.76,1.28	-	
	16,001-24,999	1.08	0.81,1.43	-	
	<16,000	1.02	0.79,1.32	-	
Oce	cupation				
	Professional office job	1		1	
	Non-manual work	0.78	0.58,1.06	0.82	0.58,1.13
	Labor work	1.22	0.95,1.57	1.35	1.01,1.79
	Skilled worker	1.15	0.85,1.55	1.29	0.93,1.78
	Unskilled worker	1.17	0.87,1.59	1.06	0.75,1.48
	Unemployed	0.85	0.71,1.14	0.90	0.68,1.18
M	arital status	0.00	0.71,1.11	0.50	0.00,1.10
1.1	Never Married	1		_	
	Currently Married	1.27	0.94,1.72	_	
	Widowed/separated/divorced	1.86	1.20,2.86	_	
Niii	mbers of Children	1.00	1.20,2.00		
114	no child	1		1	
	1-2 children	0.68	0.56,0.83	0.68	0.56,0.84
	3 and above children	0.84	0.68,1.04	0.75	0.59,0.93
E+h	nicity	0.04	0.06,1.04	0.73	0.59,0.95
Eth	Sindhi	1			
	Punjabi	1.84	1 21 2 50		
	Balochi		1.31,2.58		
	Pashtu	1.26	0.74,2.14		
	Urdu	1.68	1.12,2.51		
	Others	1.45	1.11,1.89	-	
		1.84	1.32,2.56	-	
Ho	me Status				
	Own	1	0.01.1.14	-	
	Rent	0.96	0.81,1.14	-	
	Other Arrangement	0.70	0.44,1.10	-	
Sm	oking Status				
	No	1		-	
	Yes	0.80	0.65,1.00	-	
Vis	iting Faith Healer				
	No	1		1	
	Yes	2.44	1.96,3.03	2.31	1.84,2.90

COR = unadjusted odds ratios, CI = confidence intervals.

AOR = adjusted odds ratios, only variables with p-value<0.250 in univariate analysis were entered into adjusted model using stepwise selection.

Table 3: Univariate and multivariate analysis of anxiety & depressive symptom with number of chronic diseases among adults (n=2867)

		Anxiety and	depressive sy	mptoms	
Characteristics	n (%)	COR	95% CI	AOR	95% CI
Number of chronic diseases					
None	152 (24.6)	1		1	
One	192 (23.7)	0.95	0.74,1.21	0.89	0.69,1.14
Two	181 (25.5)	1.05	0.81,1.34	0.98	0.76,1.27
Three	134 (29.8)	1.30	0.99,1.71	1.20	0.90,1.59
Four	76 (42.2)	2.24	1.58,3.17	1.92	1.33,2.78
Five +	51 (50.0)	3.06	1.99,4.70	2.62	1.66,4.13

COR = unadjusted odds ratios, CI = confidence intervals.

AOR = adjusted odds ratios, for all variables with p-value<0.250 in univariate analysis (Age, Gender, Education, Occupation, Marital status, Number of children, Ethnicity, Home status, Smoking status, Visiting faith healer).

		Reporting Item	Page Number
Title	<u>#1a</u>	Indicate the study's design with a commonly used term in the title or the abstract	01
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	02-03
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	07
Objectives	<u>#3</u>	State specific objectives, including any prespecified hypotheses	07
Study design	<u>#4</u>	Present key elements of study design early in the paper	08-09
Setting	<u>#5</u>	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	08-09
Eligibility criteria	<u>#6a</u>	Give the eligibility criteria, and the sources and methods of selection of participants.	08
	<u>#7</u>	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	09-10
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	09-11
Bias	<u>#9</u>	Describe any efforts to address potential sources of bias	07

Study size	<u>#10</u>	Explain how the study size was arrived at	08
Quantitative variables	<u>#11</u>	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	11-12
Statistical methods	<u>#12a</u>	Describe all statistical methods, including those used to control for confounding	11-12
•	#12b	Describe any methods used to examine subgroups and interactions	n/a
	#12c	Explain how missing data were addressed	13
	#12d	If applicable, describe analytical methods taking account of sampling strategy	09
	<u>#12e</u>	Describe any sensitivity analyses	n/a
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for exposed and unexposed groups if applicable.	n/a
	<u>#13b</u>	Give reasons for non-participation at each stage	n/a
	<u>#13c</u>	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	06, Table 01
	<u>#14b</u>	Indicate number of participants with missing data for each variable of interest	n/a

			1
Outcome data	<u>#15</u>	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	06-07
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3
*	#16b	Report category boundaries when continuous variables were categorized	10
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	<u>#17</u>	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Key results	<u>#18</u>	Summarise key results with reference to study objectives	13-14
Limitations	<u>#19</u>	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	4 & 17
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	18
Generalisability	#21	Discuss the generalisability (external validity) of the study results	15-17
Funding	<u>#22</u>	Give the source of funding and the role of the funders for the present study and, if applicable,	18

	for the original study on which the present article	
	is based	



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Abstract

Objectives

This study aimed to estimate the prevalence of anxiety and depressive symptoms and their association with multimorbidity and the demographic characteristics of adults, aged 30 years and above, in Karachi, Pakistan.

Design

Observational cross-sectional study

Study Setting and Participants

The study was carried out among a general population, aged 30 years and above, residing in the Gulshan-e-Iqbal town of Karachi, Pakistan. The study participants were recruited using the systematic random sampling approach, based on the inclusion criteria. The data collected from 2,867 participants was analyzed.

Main Outcome Measures

The primary outcome of the study was the prevalence of anxiety and depressive symptoms, measured with the Aga Khan University Anxiety Depression Scale (AKUADS). The secondary outcome of the study was the association of anxiety and depressive symptoms with multimorbidity, as well as with the socio-demographic characteristics of the participants, using binary logistic regression.

Results

Out of 2,867 individuals, 27.4% participants reported having anxiety and depressive symptoms. The multivariate logistic regression model revealed that the presence of multimorbidity (AOR=1.33, 95% CI: 1.11, 1.58), female gender (AOR= 2.40, 95% CI: 2.01, 2.87), illiteracy (AOR=1.51, 95% CI: 1.09, 2.07), more number of children (AOR=0.74, 95% CI: 0.59,0.93), and visiting a faith healer (AOR=2.29, 95% CI: 1.82, 2.88) were the significant factors associated with anxiety and depressive symptoms.

Conclusion

This study revealed a moderately high prevalence of anxiety and depressive symptoms among adults, aged 30 years and above, in Karachi, Pakistan. The key variables associated with anxiety and depressive symptoms were: multimorbidity, female gender, lower level of education, more number of children, and visiting faith healers.

Key words

Multimorbidity, anxiety and depression, adults

Strengths and limitations of this study

- The study sample was a large, community-based, ethnically and socio-economically diverse group of population.
- A validated screening tool (AKUADS) assessed the presence of anxiety and depressive symptoms, which enhanced the internal validity of the research.
- Inferences could not be drawn about causality of associations, due to the nature of the design.
- The study data was self-reported, hence, the results should be interpreted cautiously.

Introduction

Mental illness, anxiety, and depressive symptoms are major public health issues. Globally, 14% people suffer from mental illnesses (1). More than three quarters of these people belong to low and middle income countries(2). The magnitude of anxiety and depression is on the rise among the general population. Additionally, individuals with chronic diseases are at even higher risk of developing anxiety and depressive symptoms (3-6). In fact, depression has been ranked as the fourth leading cause of disease burden (7). Moreover, it is predicted that by the year 2020, it will be the second leading cause of disability and death, after cardio vascular disorders (7-10).

Multimorbidity is the co-occurrence of two or more chronic diseases, such as cancer, diabetes, hypertension, stroke, asthma, heart disease, arthritis, or osteoporosis within an individual (9, 11, 12). Research studies suggest that one in four adults in developed countries has multimorbidity (13, 14). (15). One study claims that 52% of people, between the ages of 21 and 84 years are suffering from multimorbidity (16), whereas, a study conducted by Garin et al., (17) in 2014 found a burden of 67% multimorbidity among elder Spanish females. Furthermore, among developing countries, in Bangladesh, the prevalence of multimorbidity is 53.8% among older adults(11),in India the burden of multimorbidity is 22% (18),while-among the Pakistani population, aged 18 years and older, it was reported as 4.9% (19). Thus, the prevalence of multimorbidity varies from 4.9% to 67% between various countries (19-21).

The reasons for variation in prevalence could be due to differences in multimorbidity definitions, number of chronic conditions included in the studies, diagnostic criteria for medical conditions, as well as the study's sample size and population characteristics. Literature suggests that the prevalence of multimorbidity increases with age (12, 22), and this burden is reported to

be more common in females. Additionally, individuals living in underprivileged areas are at a higher risk of developing multimorbidity (23).

Health care providers often face challenges when dealing with clients who have multimorbidity, along with anxiety and depressive symptoms (24, 25). As multimorbidity conditions such as diabetes, hypertension, stroke, asthma, arthritis, and osteoporosis have synergetic effects with anxiety and depression, they increase the probability of disabilities among patients (3). Moreover, Individuals with multimorbidity need to deal with multiple treatment recommendations (6). Added to that, the presence of anxiety and depression with multimorbidity leads to increase of utilization of health care facilities. This consequently leads to financial health care burdens and poorer health outcomes (2, 13, 26, 27). Thus, anxiety and depression, with multimorbidity, is linked with a 50% to 100% increase in the utilization of health services and cost (28).

Anxiety and depression are extremely common and alarmingly underdiagnosed healthcare problems, especially in low and middle income countries. In addition, they are associated with social and self-stigma, which act as a barrier in the mental help seeking behavior of individuals suffering from mental health issues, this leads to an even greater public health concern. Furthermore, anxiety and depression are specifically reported to be common in individuals with multimorbidity (3, 6). However, the studies that report these associations have mostly been conducted in high income countries. To the best of our knowledge, no such population based study has been reported from Pakistan as yet. In a resource limited setting like Pakistan, under diagnosis of mental illnesses can cause potential delay in the initiation of treatment. Hence, it is of utmost importance that anxiety and depression be screened in adults suffering from multimorbidity, in order to reduce the burden of complications and suboptimal

adherence to the treatment of multimorbidity conditions. Moreover, due to, scarcity of literature from Pakistan, requires quantification of the association between anxiety and depression with multimorbidity, within the Pakistani population is an urgent need. In this study, it was hypothesized that there is an association between anxiety and depressive symptoms and multimorbidity among the Pakistani population. Therefore, the purpose of this study was to estimate the prevalence of anxiety and depressive symptoms, and to determine their association with multimorbidity and demographic factors among adults, aged 30 years and above, in Karachi, Pakistan.

Methodology

This study was a part of a larger community based research project, titled, "The Burden of Multimorbidity, Its Patterns and Consequences on Health and Well-Being: The IMPACT Study", conducted in 2015-2016.

Study design: An observational cross-sectional study was conducted to estimate the burden of anxiety and depressive symptoms, and to identify their associated factors.

Study population: The study population comprised all adults aged 30 years and above, living in the Gulshan-e-Iqbal town, Karachi, Pakistan. This particular age group was selected for this study, as chronic medical conditions are more prevalent in this age group.

Inclusion criteria: All Persons, who were aged 30 years and above, who were the residents of the Gulshan-e-Iqbal town, Karachi, Pakistan, and who signed the consent form to take part in the study.

Sample size calculation: To meet the objective of this study, the sample size was calculated using an online version of Open Epi calculator. The prevalence of anxiety and depression is reported to be 30% to 50% among adults in Pakistan (29, 30). With a 2% margin of error and 95% confidence level, the required sample size was 2,401 participants. Similarly, for attaining the secondary objective (association of anxiety and depressive symptoms with multimorbidity), keeping the confidence interval of 95%, 90% power, 1:1 ratio of non-depressed and depressed individuals, with odds ratio of 1.55, and proportion of multimorbidity among non-depressed was taken as 10% (Smith et al., 2014), the required sample size was 2,148 individuals. In order to account for missing values, the higher sample size (2401) was chosen. Ultimately, however, 3,250 individuals were recruited for data collection.

Sampling Technique: The present study was conducted in the Gulshan-e-Iqbal town of Karachi, Pakistan. A sample of 3,250 participants was recruited using the systematic random sampling technique. This sample was achieved by using proportionate estimates of the number of individuals in 13 Union Councils (UCs) in the selected town. The Proportionate allocation method was used in order to allocate appropriate weightage to each UC. Within each UC, blocks of houses were selected with a random start, where every 109th (kth sampling interval) household was selected. Individuals within these households, who met the eligibility criteria, were included in the study.

Data Collection: Data were collected from participants by interviewing them, with the help of a structured questionnaire; the questionnaire was developed after a thorough literature review. The questionnaire was designed to collect data related to socio demographic information including age, gender, marital status, educational status, employment status, mother tongue, number of family members and information about housing, presence of any chronic disease, and living conditions of each participant. Participants were interviewed by trained data collectors; the anthropometric measurements, as well as Blood Pressure were measured by trained health professionals, mainly included doctors and nurses, who were involved in data collection.

Dependent variable: The Aga Khan University Anxiety Depression Scale (AKUADS) was used to assess the anxiety and depressive symptoms of the participants. This study used the Urdu version of the AKUADS, which had been validated in a previous research (31). The value of the reliability coefficient tool in the study population was 0.93. This tool had a total of 25 questions and for each of the questions the participants could choose an answer from Never (scored as 0), Sometimes (scored as 1), Often (scored as 2), Always (scored as 3). The cumulative cutoff score

of 20 or greater on this scale was used to label anxiety and depression. At a cutoff score of 20, the AKUADS had a sensitivity of 66% and a specificity of 79% (31, 32).

Independent Variables: The presence of disease was assessed by a combination of self-reported diagnosis, medication use, and laboratory findings. Self-reported disease was determined by the question: "Have you ever been told by a doctor, nurse, or other health professional that you have hypertension, obesity, dyslipidemia, diabetes, heart diseases (Myocardial Infarction and/or chronic ischemic heart diseases), stroke, migraines, asthma and COPD, anemia, thyroid disease, diseases of bones and joints, dyspepsia/peptic ulcer, hepatitis B or C, chronic kidney diseases including stones, cancer, and/or disability?".

Individuals with 2 or more chronic diseases (excluding anxiety and depression) were labeled as having 'multimorbidity' and others who reported one or no chronic medical disease were considered as having 'no multimorbidity'. Set criteria were used to define chronic diseases, such as hypertension, obesity, diabetes, and dyspepsia. A person was said to be hypertensive if that person had a high systolic BP (>140 mm Hg) or a high diastolic BP (>90 mm Hg). A person was considered obese if they had a calculated BMI ≥ 30.0 kg/m². A person was said to be diabetic if their blood glucose level was ≥ 200 mg/dl. A person was considered having dyspepsia if they had four or more symptoms of dyspepsia for at least 6 months, based on the Leeds Dyspepsia Questionnaire (LDQ).

Beside disease related variables, other socio demographic variables were also measured, such as household income, occupation, and education. This variable was initially taken as continuous variable, such as what is your monthly income (in Pakistani Rupees). Then it was further classified into quintiles, i.e. < 16,000, 16,001-24,999, 25,000-39,999, 40,000-54,999 and 55,000

rupees and above. The occupation of all the participants was also assessed as a categorical variable and had categories such as unemployed, unskilled worker, skilled worker, labor worker, non-manual worker and professional office job. Data on education were collected as total number of years of full education, which was then categorized into five categories No education (0 years or those who never attended school), Primary (1-5 years), Secondary (6-10 years), Higher education (11-14 years)

Postgraduate (≥15 years)

Ethical considerations: The study's proposal was approved by The Institutional Review Board (IRB) of the Dow University of Health Sciences, reference number: Ref: IRB-554/DUHS/Approval/2015/04. Only individuals who provided written informed consent were interviewed. A referral plan for counseling was made for participants who scored 20 and above on the AKUADS scale.

Statistical Analysis: Variables were pre-coded and data were entered and analyzed in the SPSS version 19.0. Descriptive statistics were calculated in the form of frequencies and percentages for categorical variables. Descriptive statistics were calculated in order to estimate the prevalence of anxiety and depressive symptoms. Univariate and multivariate binary logistics regressions were used to assess the associations between anxiety and depressive symptoms and multimorbidity and odd ratios and their 95% confidence intervals were also calculated. The multivariate model was adjusted only for variables with p-values <0.250 in univariate analysis, using a step-wise logistic regression method, following the Hosmer and Lemeshow protocol (33). Moreover, this manuscript has followed STROBE cross sectional reporting guidelines (34).

Patient and public involvement: In the current study, patients were not involved in the research question, study design, outcome measures, and recruitment.



Results

A total of 3,250 participants were interviewed. However, the data were analyzed using information from 2,867 study participants. Of the total, 383 participants were excluded due to missing information on the variables: anxiety & depression symptoms (n=06), presence of multimorbidity (n=09), respondent age (n=06), gender (n=08), education (n=48), income (n=81), occupation (n=72), marital status (n=05), number of children (n=67), ethnicity (n=09), home status (n=14), smoking status (n=66), and visiting faith healer (n=93).

The mean age of the 2,867 study participants was 45.5 years (SD ±11.7 years). The male/female ratio was approximately equal, males 51.5 % (n=1,477), females 48.5% (n=1,390). Regarding the educational level of the participants, 14% (n=404) had no formal education, 38.3% (n=1098) had higher education, and 20.4% (n=585) had postgraduate education. In addition, 22.3% (n=638) reported their monthly household income to be less than 16,000 rupees, while 18.2% (n=523) claimed their monthly income to be more than 55,000 rupees. The majority of participants 42% (n=1205) had professional jobs, 14% (n=389) were laborers, and 17% (n=484) participants were unemployed. The study participants reported anxiety and depressive symptoms, and multimorbidity as27.4% (n=786) and 50.2% (n=1440), respectively. The sociodemographic and other characteristics of the participants are shown in Table 1.

The adjusted model revealed that participants who had multimorbidity had 33% increased odds of being anxious and depressed (AOR=1.33, 95% CI: 1.11, 1.58), as compared to those who did not report multimorbidity. Moreover, the odds of having anxiety and depressive symptoms were 2.40 times higher among females, as compared to male participants (AOR=2.40, 95% CI:2.01, 2.87). And the odds of having anxiety and depressive symptoms were 51% higher among participants who had no formal education (AOR=1.51, 95% CI: 1.09, 2.07), as

compared to participants who had postgraduate education. Furthermore, the odds of being anxious and depressed were 1.34 times higher among participants who did labor work as compared to participants who were doing professional office jobs (AOR=1.34, 95% CI: 1.00, 1.79). Also, study participants who had 1 to 2 children were at 32% reduced odds (AOR=0.68, 95% CI: 0.56, 0.84), and those who had more than two children were at 26% reduced odds (AOR=0.74, 95% CI: 0.59, 0.93) of having anxiety and depressive symptoms, as compared to participants who had no children. Furthermore, Subjects belonging to the Punjabi ethnicity (AOR=1.66, 95% CI: 1.16, 2.37), had 66% increased odd of being anxious and depressed as compared to Sindhi subjects. In addition, subjects who were visiting a faith healer were 2.29 times (AOR=2.29, 95% CI: 1.82, 2.88) odds of exhibiting anxiety and depressive symptoms, as compared to participants who did not visit a faith healer (Table 2).

Table 3 shows the estimated association of anxiety and depressive symptoms and the number of chronic diseases. The anxiety and depressive symptoms were significantly associated with increasing number of chronic diseases. The odds of anxiety and depressive symptoms were highest among individuals with four chronic diseases (AOR=1.92, 95% CI: 1.33, 2.78), and more than four chronic diseases (AOR=2.62, 95% CI: 1.66, 4.13), as compared with healthy individuals, when adjusted for other variables (Table 3).

Discussion

This study showed that nearly one fourth of the study participants had symptoms of anxiety and depression. Moreover, it illustrated that the presence of multimorbidity, female gender, lower level of education, more number of children, ethnicity and visiting a faith healer were significantly associated with anxiety and depressive symptoms.

The current study used a screening tool (AKUADS) to assess the presence of anxiety and depressive symptoms. According to the findings, the overall prevalence of anxiety and depressive symptoms was 27.4%. This has previously been reported to be around 10% and 44%, in developed and developing countries, respectively (35, 36). Islam et al., in their study conducted in 2003 (37), found a 28% prevalence of depression among the Bangladesh population. In the United States, the prevalence of anxiety and depression was reported to be 16.2% (38). Papadopoulos et al.,(39) reported that the prevalence of depression in Greece as27%. Whereas in India, the prevalence of depression was found to be 28% (40). However, in Pakistan, the prevalence of depression and anxiety has been found to be around 30% to 50 %. (29, 35, 36, 41). A plausible reason for the difference in the prevalence of anxiety and depression could be different inclusion criteria, sample sizes, recruitment methods, various screening tools, and cutoff points that were employed in these diverse studies (21).

In the past decade, several research studies have established a strong relationship between anxiety and depression and multimorbidity (4, 6, 9, 42). The findings of the present study were in concurrence with the previous studies, showing a significant association between anxiety and depression, and multimorbidity (6, 9, 43-46). A probable reason could be that mental illness is linked with unhealthy habits, such as smoking, poor self-care, lack of physical activities, and poor medication compliance (44, 47).

In the present study, anxiety and depressive symptoms were found to be strongly associated with females. The prevalence of anxiety and depressive symptoms were found to be 2.5 times higher in females than in males. Likewise, previous studies have also revealed a positive association between anxiety, depression, and gender. A research conducted by Mirza and Jenkin (41) found that the prevalence of anxiety and depressive symptoms were 29-66% among females, as compared to 10-33% in males, Plausible reasons for the higher prevalence of anxiety and depression among women could be biological factors, socio-economical disadvantages, deprivation of social status, maladaptive coping styles, and lack of a support system for females in our country (48).

The current study also found illiteracy as one of the potential risk factors among participants. Similarly, previous studies have found a strong association between low levels of education, and anxiety and depressive symptoms (49, 50). Among the literate population, education could be one of the factors that facilitates adaptive coping skills amongst them, and enables them to deal with distress situations and in improving their self-confidence, self-efficacy, social skills building and developing a sense of control over the environment (51).

According to the findings of the current study, participants who bore more children were less likely to develop anxiety and depressive symptoms. The plausible reason could be that parents tend to positively engage with their children and to be bound with their lives children by giving them continuous love, time, supports and commitment, which can all be coping strategies against distress. More number of children can also act as a buffer, considering the cultural dimension of the south Asian population where older children serve as a financial security for the family (52). Moreover, they also perform the role of caretaker, and/or may contribute to family house hold chores. This provides positive hope to the family that their future financial and social

security is warranted and, thus, decreases anxiety and depression. In contrast, other studies have found that having more children is a risk factor for anxiety and depression among women (49, 53).

Our study also revealed that ethnicity of a participant is linked with anxiety and depressive symptoms. Subjects who were Punjabi were more likely to have anxiety and depressive symptoms. Consistent findings were reported by former studies that ethnicity was a significant risk factor for depression (54, 55). However, another study reported no association between these variables (53).

A notable finding of the present study was that visiting a faith healer was positively associated with anxiety and depression among both genders. In the Pakistani culture, distressed individuals generally seek help from traditional healers or faith healers prior to visiting a doctor or a psychiatrist for their illness. A few probable reasons why people visit faith healers could their easy accessibility, availability, and affordability, cultural beliefs and the predominant stigma attached to the notion of mental illness (53, 56). Moreover, in Pakistan, many people believe that mental illnesses are due to wrong doings, being possessed, witchcraft, and evil spirits; hence, the affected population consults these faith healers rather than doctors. Our result is consistent with a past study, where it was reported that sixteen percent of the Pakistani population first approaches faith healers for their illness (57).

Strengths and Limitations

This is probably the first research that has determined an association of anxiety and depressive symptoms with multimorbidity, among the population in Pakistan. Due to the cross-sectional nature of study inferences could not be determined about the causality of the

relationship. Potential risk factors, such as, family history of psychiatric disorders, marital dissatisfaction, domestic violence, maladaptive coping, current life stressors, and death of a loved one, could not be addressed in the current study. Moreover, this study was based on self-reported information about multimorbidity, and anxiety and depression.

Conclusion

This study suggests that almost one quarter of the study population had anxiety and depressive symptoms. Among females, the anxiety and depressive symptoms are twice as common as compared to males. Early prevention and screenings are the key measures for preventing the rising burden of mental disorders, when dealing with chronic physical conditions. Therefore, there is a dire need to create awareness regarding identification of symptoms of mental illness and to develop a proper referral system for essential treatment at the early stage of the disease, to avoid delayed presentation when the disease is more advanced.

Author Contributions

KS and SF conceived the research question and the design of this project. SF conducted all the literature reviews and manuscript drafting and reviewing, as well as took part in data collection. MTK and SZ helped in the data analysis, preparation of tables, and reviewed the manuscript. KS supervised the research project and conducted the final editing and review of the manuscript. The final version of this manuscript was seen and approved by all contributors.

Conflicts of Interest

None

Data availability statement

The data is available on request from the corresponding author.

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References

- 1. Yatham S, Sivathasan S, Yoon R, da Silva TL, Ravindran AV. Depression, anxiety, and post-traumatic stress disorder among youth in low and middle income countries: a review of prevalence and treatment interventions. Asian journal of psychiatry. 2018;38:78-91.
- 2. Jordans MJ, Kaufman A, Brenman NF, Adhikari RP, Luitel NP, Tol WA, et al. Suicide in South Asia: a scoping review. BMC psychiatry. 2014;14(1):358.
- 3. Deschênes SS, Burns RJ, Schmitz N. Associations between depression, chronic physical health conditions, and disability in a community sample: A focus on the persistence of depression. Journal of affective disorders. 2015;179:6-13.
- 4. Winkler P, Horáček J, Weissová A, Šustr M, Brunovský M. Physical Comorbidities in Depression Co-Occurring with Anxiety: A Cross Sectional Study in the Czech Primary Care System. International journal of environmental research and public health. 2015;12(12):15728-38.
- 5. Levinson D, Karger CJ, Haklai Z. Chronic physical conditions and use of health services among persons with mental disorders—results from the Israel National Health Survey. General hospital psychiatry. 2008;30(3):226-32.
- 6. Gunn JM, Ayton DR, Densley K, Pallant JF, Chondros P, Herrman HE, et al. The association between chronic illness, multimorbidity and depressive symptoms in an Australian primary care cohort. Social psychiatry and psychiatric epidemiology. 2012;47(2):175-84.
- 7. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic disease and decrements in health: Evidence from the World Health Surveys. Lancet. 2007;369:851-8.
- 8. Mathers C, Fat DM, Boerma JT. The global burden of disease: 2004 update: World Health Organization; 2008.
- 9. O'Connor K, Vizcaino M, Ibarra JM, Balcazar H, Perez E, Flores L, et al. Multimorbidity in a Mexican Community: Secondary Analysis of Chronic Illness and Depression Outcomes. International journal of nursing (New York, NY). 2015;2(1):35.
- 10. WHO. Depression and other common mental disorders: global health estimates. 2017.
- 11. Khanam MA, Streatfield PK, Kabir ZN, Qiu C, Cornelius C, Wahlin Å. Prevalence and patterns of multimorbidity among elderly people in rural Bangladesh: a cross-sectional study. Journal of health, population, and nutrition. 2011;29(4):406.
- 12. Liddy C, Blazkho V, Mill K. Challenges of self-management when living with multiple chronic conditions Systematic review of the qualitative literature. Canadian Family Physician. 2014;60(12):1123-33.
- 13. Ahmadi B, Alimohammadian M, Yaseri M, Majidi A, Boreiri M, Islami F, et al. Multimorbidity: Epidemiology and Risk Factors in the Golestan Cohort Study, Iran: A Cross-Sectional Analysis. Medicine. 2016;95(7):e2756.
- 14. Alaba O, Chola L. The social determinants of multimorbidity in South Africa. Int J Equity Health. 2013;12(1):1-10.
- 15. Chatterji S, Byles J, Cutler D, Seeman T, Verdes E. Health, functioning, and disability in older adults—present status and future implications. The Lancet. 2015;385(9967):563-75.
- 16. Aarts S, van den Akker M, Bosma H, Tan F, Verhey F, Metsemakers J, et al. The effect of multimorbidity on health related functioning: Temporary or persistent? Results from a longitudinal cohort study. Journal of psychosomatic research. 2012;73(3):211-7.
- 17. Garin N, Olaya B, Perales J, Moneta MV, Miret M, Ayuso-Mateos JL, et al. Multimorbidity patterns in a national representative sample of the Spanish adult population. PloS one. 2014;9(1).

- 18. Akinsulore A, Esimai OA, Afolabi OT, Aloba OO, Mapayi BM. Prevalence and factors associated with depressive symptoms among Yoruba adults in a semi-urban community in South-Western Nigeria. Journal of Behavioral Health. 2015;4(3):81-6.
- 19. Afshar S, Roderick PJ, Kowal P, Dimitrov BD, Hill AG. Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys. BMC public health. 2015;15(1):1.
- 20. Roberts K, Rao D, Bennett T, Loukine L, Jayaraman G. Prevalence and patterns of chronic disease multimorbidity and associated determinants in Canada. Health Promotion. 2015;35(6):87-94.
- 21. Taylor AW, Price K, Gill TK, Adams R, Pilkington R, Carrangis N, et al. Multimorbidity-not just an older person's issue. Results from an Australian biomedical study. BMC public health. 2010;10(1):1.
- 22. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Ageing research reviews. 2011;10(4):430-9.
- 23. Orueta JF, Nuño-Solinís R, García-Alvarez A, Alonso-Morán E. Prevalence of multimorbidity according to the deprivation level among the elderly in the Basque Country. BMC public health. 2013;13(1):918.
- 24. Roca M, Gili M, Garcia-Garcia M, Salva J, Vives M, Campayo JG, et al. Prevalence and comorbidity of common mental disorders in primary care. Journal of affective disorders. 2009;119(1):52-8.
- 25. Naqvi H, Khan MM. Depression in primary care: difficulties and paradoxes. JPMA 2005;55(9):393.
- 26. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. The European journal of general practice. 2008;14(sup1):28-32.
- 27. Lockett H, Lai J, Tuason C, Jury A, Fergusson D. Primary healthcare utilisation among adults with mood and anxiety disorders: an analysis of the New Zealand Health Survey. Journal of Primary Health Care. 2018;10(1):68-75.
- 28. Simon GE, VonKorff M, Barlow W. Health care costs of primary care patients with recognized depression. Archives of general psychiatry. 1995;52(10):850-6.
- 29. Ali B, Amanullah S. Prevalence of anxiety and depression in an urban squatter settlement of Karachi. JCPSP, Journal of the College of Physicians and Surgeons-Pakistan. 2000;10(1):4-6.
- 30. Waheed A, Hameed K, Khan AM, Syed J, Mirza AI. The burden of anxiety and depression among patients with chronic rheumatologic disorders at a tertiary care hospital clinic in Karachi, Pakistan. JPMA The Journal of the Pakistan Medical Association. 2006;56(5):243-7.
- 31. Ali BS. Validation of an indigenous screening questionnaire for anxiety and depression in an urban squatter settlement of Karachi. J Coll Physicians Surg Pak. 1998;8:207-11.
- 32. Ali BS, Reza H. Development of an indigenous screening instrument in Pakistan: the Aga Khan University Anxiety and Depression Scale. JPMA 1998;48:261-5.
- 33. Hosmer Jr DW, Stanley Lemeshow, and Rodney X Sturdivant. Applied logistic regression: John Wiley & Sons; 2013.
- 34. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS medicine. 2007;4(10):e296.
- 35. Luni FK, Ansari B, Jawad A, Dawson A, Baig SM. Prevalence of depression and anxiety in a village in Sindh. J Ayub Med Coll Abbottabad. 2009;21(2):68-72.
- 36. Muhammad Gadit AA, Mugford G. Prevalence of depression among households in three capital cities of Pakistan: need to revise the mental health policy. Plos one. 2007;2(2):e209.
- 37. Islam MM, Ali M, Ferroni P, Underwood P, Alam MF. Prevalence of psychiatric disorders in an urban community in Bangladesh. General hospital psychiatry. 2003;25(5):353-7.

- 38. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003;289(23):3095-105.
- 39. Papadopoulos F, Petridou E, Argyropoulou S, Kontaxakis V, Dessypris N, Anastasiou A, et al. Prevalence and correlates of depression in late life: a population based study from a rural Greek town. Int J Geriatr Psychiatry. 2005;20(4):350-7.
- 40. Patel V, Prince M. Ageing and mental health in a developing country: who cares? Qualitative studies from Goa, India. Psychological Medicine. 2001;31(01):29-38.
- 41. Mirza I, Jenkins R. Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review. Bmj. 2004;328(7443):794.
- 42. Smith DJ, McLean G, Martin D, Langan MJ, Guthrie B, Gunn J, et al. Depression and multimorbidity: a cross-sectional study of 1,751,841 patients in primary care. The Journal of clinical psychiatry. 2014;75(11):1202-8.
- 43. Patten SB. Long-term medical conditions and major depression in a Canadian population study at waves 1 and 2. Journal of affective disorders. 2001;63(1):35-41.
- 44. Patten SB. An analysis of data from two general health surveys found that increased incidence and duration contributed to elevated prevalence of major depression in persons with chronic medical conditions. Journal of clinical epidemiology. 2005;58(2):184-9.
- 45. Patten SB, Wang JL, Williams JV, Currie S. Descriptive epidemiology of major depression in Canada. Canadian journal of psychiatry. 2006;51(2):84.
- 46. Spangenberg L, Forkmann T, Braehler E, Glaesmer H. The association of depression and multimorbidity in the elderly: implications for the assessment of depression. Psychogeriatrics. 2011;11(4):227-34.
- 47. Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. Biological psychiatry. 2003;54(3):216-26.
- 48. Zahidie A, Jamali T. An overview of the predictors of depression among adult Pakistani women. Journal of the College of Physicians and Surgeons Pakistan. 2013;23(8):574.
- 49. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. Psychological medicine. 2000;30(02):395-402.
- 50. Lovisi GM, Lopez J, Coutinho ESF, Patel V. Poverty, violence and depression during pregnancy: a survey of mothers attending a public hospital in Brazil. Psychological Medicine. 2005;35(10):1485-92.
- 51. Harpham T. Urbanization and mental health in developing countries: a research role for social scientists, public health professionals and social psychiatrists. Social science & medicine. 1994;39(2):233-45.
- 52. Hussain M, and Adam Saud. Socio-Economic Determinants of Working Children: Evidence from Capital Territory of Islamabad, Pakistan. Pakistan Administrative Review. 2017;1(2):145-58.
- 53. Nisar N, Billoo N, Gadit A. Prevalence of depression and the associated risks factors among adult women in a fishing community. JPMA. 2004;54(10):519-25.
- 54. Costello DM, Swendsen J, Rose JS, Dierker LC. Risk and protective factors associated with trajectories of depressed mood from adolescence to early adulthood. Journal of consulting and clinical psychology. 2008;76(2):173.
- 55. Lankarani MM, Assari S. Association between number of comorbid medical conditions and depression among individuals with diabetes; race and ethnic variations. Journal of Diabetes & Metabolic Disorders. 2015;14(1):1.
- 56. Mishra N, Nagpal SS, Chadda RK, Sood M. Help-seeking behavior of patients with mental health problems visiting a tertiary care center in north India. Indian journal of psychiatry. 2011;53(3):234.
- 57. Mubbashar M, Saeed K. Development of mental health services in Pakistan. Eastern Mediterranean health journal. 2001;7:392-6.

Table 1: Socio-demographic and other characteristics of participants (n=2867)

Characteristics	(0/)
Characteristics	n (%)
Anxiety and depressive sympt	
No	2081 (72.6)
Yes	786 (27.4)
Presence of multimorbidity	
No	1427 (49.8)
Yes	1440 (50.2)
Age	
30-39 years	1062 (37.0)
40-49 years	816 (28.5)
50-59 years	570 (19.9)
60-69 years	293 (10.2)
≥70 years	126 (4.4)
Gender	
Male	1477 (51.5)
Female	1390 (48.5)
Education	L .
No education	404 (14.1)
Primary	133 (4.6)
Secondary	647 (22.6)
Higher/Graduation	1098 (38.3)
Post-graduate	585 (20.4)
Income	
<16,000	638 (22.3)
16,001-24,999	426 (14.9)
25,000-39,999	636 (22.2)
40,000-54,999	644 (22.5)
>55,000	523 (18.2)
Occupation	
Unemployed	484 (16.9)
Unskilled worker	243 (8.5)
Skilled worker	250 (8.7)
Labor work	389 (13.6)
Non-manual work	296 (10.3)
Professional office job	1205 (42)
Marital status	1203 (42)
mainai status	

Never Married	272 (9.5)
Currently Married	2437 (85.0)
Widowed/Separated/Divorced	158 (5.5)

Numbers of Children

No child	1250 (43.6)
1-2 children	974 (34.0)
3 and above children	643 (22.4)

Ethnicity

Sindhi	402 (14.0)
Punjabi	318 (11.1)
Balochi	94 (3.3)
Pashtu	176 (6.1)
Urdu	1534 (53.5)
Others	343 (12.0)

Home Status

Own	1595 (55.6)
Rent	1155 (40.3)
Other Arrangement	117 (4 1)

Smoking Status

No	2323 (81.0)
Yes	544 (19.0)

Visiting Faith Healer

No	2471 (86.2)
Yes	396 (13.8)

Table 2: Univariate and multivariate analysis of factors associated with anxiety & depressive symptoms among adults (n=2867)

		Anxiety and	depressive symp	toms
Characteristics	COR	95% CI	AOR	95% CI
Presence of multimorbidity				
No	1		1	
Yes	1.39	1.18,1.64	1.33	1.11,1.58
Age		•		
30-39 years	1		-	
40-49 years	0.95	0.77,1.77	-	
50-59 years	1.14	0.92,1.40	-	
60-69 years	1.02	0.78,1.40	-	
≥70 years	1.26	0.85,1.88	-	
Gender				
Male	1		1	
Female	2.58	2.17,3.05	2.40	2.01,2.87
Education				
Post-graduate	1		1	
Higher/Graduation	0.89	0.71,1.13	0.86	0.67,1.09
Secondary	1.15	0.89,1.48	1.05	0.78,1.40
Primary	1.22	0.81,1.85	1.11	0.70,1.77
No education	1.95	1.48,2.57	1.51	1.094,2.0
ncome				
>55,000	1		-	
40,000-54,999	0.91	0.69,1.17	_	
25,000-39,999	0.99	0.76,1.28	-	
16,001-24,999	1.08	0.81,1.43	-	
<16,000	1.02	0.79,1.32		
Occupation				
Professional office job	1		1	
Non-manual work	0.78	0.58,1.06	0.81	0.58,1.13
Labor work	1.22	0.95,1.57	1.34	1.00,1.79
Skilled worker	1.15	0.85,1.55	1.29	0.93,1.78
Unskilled worker	1.17	0.87,1.59	1.06	0.75,1.48
Unemployed	0.85	0.71,1.14	0.90	0.68,1.18
Marital status				
Currently Married	1		1	
Never Married	0.78	0.58,1.05	0.87	0.62,1.17
Widowed/separated/divorced	1.45	1.03,2.03	1.02	0.72,1.48
Numbers of Children				
no child	1		1	
1-2 children	0.68	0.56,0.83	0.68	0.56,0.84

3 and above children	0.84	0.68,1.04	0.74	0.59,0.93
Ethnicity				
Sindhi	1		1	
Punjabi	1.84	1.31,2.58	1.66	1.16,2.37
Balochi	1.26	0.74,2.14	1.32	0. 76,2.30
Pashtu	1.68	1.12,2.51	1.39	0.90,2.13
Urdu	1.45	1.11,1.89	1.35	1.00,1.81
Others	1.84	1.32,2.56	1.52	1.07,2.17
Home Status				
Own	1		-	
Rent	0.96	0.81,1.14	-	
Other Arrangement	0.70	0.44,1.10	-	
Smoking Status				
No	1		-	
Yes	0.80	0.65,1.00	-	
Visiting Faith Healer				
No	1		1	
Yes	2.44	1.96,3.03	2.29	1.82,2.88

COR = unadjusted odds ratios, CI = confidence intervals.

AOR = adjusted odds ratios, only variables with p-value<0.250 in univariate analysis were entered into adjusted model using stepwise selection(Presence of multimorbidity, Gender, Education, Occupation, Marital status, Number of children, Ethnicity, Visiting faith healer).

Table 3: Univariate and multivariate analysis of anxiety & depressive symptom with number of chronic diseases among adults (n=2867)

	Anxiety and depressive symptoms				
Characteristics	n (%)	COR	95% CI	AOR	95% CI
Number of chronic	diseases				
None	152 (24.6)	1		1	
One	192 (23.7)	0.95	0.74,1.21	0.89	0.69,1.14
Two	181 (25.5)	1.05	0.81,1.34	0.98	0.76,1.27
Three	134 (29.8)	1.30	0.99,1.71	1.20	0.90,1.59
Four	76 (42.2)	2.24	1.58,3.17	1.92	1.33,2.78
Five +	51 (50.0)	3.06	1.99,4.70	2.62	1.66,4.13

COR = unadjusted odds ratios, CI = confidence intervals.

AOR = adjusted odds ratios, for all variables with p-value<0.250 in univariate analysis (Age, Gender, Education, Occupation, Marital status, Number of children, Ethnicity, Home status, Smoking status, Visiting faith healer).

		Reporting Item	Page Number
Title	<u>#1a</u>	Indicate the study's design with a commonly used term in the title or the abstract	01
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	02-03
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	07
Objectives	#3	State specific objectives, including any prespecified hypotheses	07
Study design	<u>#4</u>	Present key elements of study design early in the paper	08-09
Setting	<u>#5</u>	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	08-09
Eligibility criteria	<u>#6a</u>	Give the eligibility criteria, and the sources and methods of selection of participants.	08
	<u>#7</u>	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	09-10
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	09-11
Bias	<u>#9</u>	Describe any efforts to address potential sources of bias	07

Study size	<u>#10</u>	Explain how the study size was arrived at	08
Quantitative variables	<u>#11</u>	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	11-12
Statistical methods	<u>#12a</u>	Describe all statistical methods, including those used to control for confounding	11-12
•	#12b	Describe any methods used to examine subgroups and interactions	n/a
	#12c	Explain how missing data were addressed	13
	#12d	If applicable, describe analytical methods taking account of sampling strategy	09
	<u>#12e</u>	Describe any sensitivity analyses	n/a
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for exposed and unexposed groups if applicable.	n/a
	<u>#13b</u>	Give reasons for non-participation at each stage	n/a
	<u>#13c</u>	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	06, Table 01
	<u>#14b</u>	Indicate number of participants with missing data for each variable of interest	n/a

			1
Outcome data	<u>#15</u>	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	06-07
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3
*	#16b	Report category boundaries when continuous variables were categorized	10
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	<u>#17</u>	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Key results	<u>#18</u>	Summarise key results with reference to study objectives	13-14
Limitations	<u>#19</u>	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	4 & 17
Interpretation	<u>#20</u>	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	18
Generalisability	#21	Discuss the generalisability (external validity) of the study results	15-17
Funding	<u>#22</u>	Give the source of funding and the role of the funders for the present study and, if applicable,	18

for the original study on which the present article	
is based	

