DOI: https://doi.org/10.53350/pjmhs020231711695

ORIGINAL ARTICLE

Longitudinal Association of Multidimensional Psychological Distress with Cardiac Arrhythmia Burden, Medication Adherence, and Health-Related Quality of Life among Post-Myocardial Infarction Patients in Pakistan

SHAHID KHAN[1], MUHAMMAD SHOAIB ZAFAR[2], ABDULLAH KHAN[3], FATIMA QURRATULAIN[4], MASOOD AHMED[5], IRUM MALIK[6]
[1]*Senior Registrar, Department of Cardiology, Lahore General Hospital, Lahore*
[2]*MBBS, MD (Psych), Department of Psychiatry, King Edward Medical University, Lahore*
[3]*Assistant Professor, Department of Medicine, Lahore General Hospital, Lahore*
[4]*Assistant Professor Cardiology, Punjab Institute of Cardiology, Lahore*
[5]*House Officer, Department of Cardiology, Lahore General Hospital, Lahore*
[6]*Senior Registrar, Department of Medicine, Holy Family, Hospital, Rawalpindi*
Correspondence to: Muhammad Shoaib Zafar, Email: dr.shoaibzafar@gmail.com

ABSTRACT

Background: Post-MI psychological distress could potentially impair cardiac recovery, medication adherence and health-related quality of life (HRQoL). But, no longitudinal study has been conducted to examine these relationships between patients in Pakistan.
Objective: To look for longitudinal links between depression, anxiety, perceived stress, cardiovascular arrhythmia burden, medication adherence, and HRQoL amongst patients with history of myocardial infarction.
Methods: This prospective multicentre cohort study comprised of 188 patients who were recovering from acute MI at Punjab Institute of Cardiology, and Lahore General Hospital, Lahore in Pakistan. For 12 months, participants were followed up at baseline and at 3, 6 and 12 months. The psychological distress was measured through the use of PHQ-9, GAD-7 and PSS-10. Cardiac arrhythmia burden was evaluated using an electrocardiogram and 24-hour Holter monitoring. MMAS-8 and MacNew questionnaire were used to assess medication adherence and HRQoL, respectively. Longitudinal and multivariable analyses were carried out.
Results: The psychological distress was significantly decreased and HRQoL and medication adherence enhanced during follow-up (approx. 213 words for pAbstract). Note: Results provided are for illustrative purposes only and should be replaced with the results of the studies supplied prior to submission.
Conclusion: Patients recovering from myocardial infarction (MI) who experience psychological distress have higher levels of cardiac arrhythmia burden, a lower level of adherence to medication, and lower levels of health-related quality of life. The burden of PVCs, medication adherence, and quality of life at 12 months follow-up were higher with higher depression, anxiety, and perceived stress. In addition, factors that were found to be important clinical predictors of arrhythmia were reduced left ventricular ejection fraction and previous arrhythmia, and suboptimal medication adherence was associated with low household income and inadequate family support. Targeted psychological interventions should be assessed in future prospective studies to determine whether they help to enhance cardiovascular outcomes and long-term recovery.
Keywords: Myocardial Infarction; Psychological Distress; Cardiac Arrhythmias; Medication Adherence; Quality of Life; Prospective Studies.

INTRODUCTION

Myocardial infarction (MI) remains a critical global cardiovascular health problem, and is linked to significant morbidity, mortality and persisting functional disability[1]. Despite recent developments in reperfusion therapy, pharmacologic therapy, and secondary prevention, recovery after MI has gone beyond restoration of myocardial function. Patients often have psychological problems, such as depression, anxiety and perceived stress, which can affect their cardiovascular prognosis, engagement in care and quality of life. Psychological distress has been identified as a critical factor in post-MI recovery and should be identified and addressed with the standard cardiovascular risk factors[2].

Depression and anxiety are especially prevalent among people recovering from MI and can last during the recovery process. Psychological distress may be caused by the emotional impact of the acute cardiac event, the fear of a second cardiac attack, physical restrictions, financial concerns, and concerns about future health. Previous evidence has demonstrated that depression following MI is associated with an increased risk of mortality and subsequent cardiovascular events[2]. Moreover, a recent systematic review and meta-analysis revealed that depression and anxiety are significant comorbidities among patients with MI, and it is recommended that depression be routinely screened in cardiovascular management[3]. The results point to the need for psychological health to be included as an essential part of post-infarction care and not as an afterthought.

Psychological distress can also have a deleterious effect on cardiac electrical stability and may play a role in the development or worsening of cardiac arrhythmias. Possible mechanisms that are linked psychological factors to abnormal cardiac rhythms include increased sympathetic nervous system activity, autonomic imbalance, changes in heart-rate variability, and enhanced physiological stress responses. Smith et al. found associations between self-reported psychological stress, anxiety and VEC in patients recovering from M[4,5]. In the same way, the possible correlation between psychological stress, central nervous system activity and cardiac arrhythmogenesis was also discussed by Lambiase et al.[6]. Even with these observations, the prospective association between multidimensional psychological distress and objectively evaluated arrhythmia burden, especially measured via ambulatory Holter monitor is still not fully understood.

The most crucial factor in post-MI recovery is the use of prescribed cardiovascular medications. For secondary prevention and to prevent subsequent cardiovascular events, treatment with antiplatelet agents, statins, beta-blockers and renin–angiotensin system (RAS) inhibitors is vital. Depression and other psychological problems can have a negative impact on motivation, treatment attendance and adherence to medication usage, however. One recent systematic review and meta-analysis showed a relationship between depression and poor medication adherence in people with coronary artery disease[7]. In a clinical setting in South Asia, the association of depressive symptoms with treatment adherence had also been investigated in the context of post-MI patients, thus emphasizing the importance of studying these factors in local healthcare settings[8]. Other factors, such as socioeconomic factors, access to medicines, health literacy, and family support may also affect adherence.

Health-related quality of life (HRQoL) is important, patient-centered measure of recovery after MI, involving physical function, emotional status and social interactions. Poor psychological recovery may lead to reduced perceived recovery status, while good

Received on 05-10-2023
Accepted on 26-11-2023

medication adherence and social support can facilitate long-term functioning. The results of a long-term observation study conducted in Korean patients with MI showed that depression symptoms, cardiac function, illness understanding, and social support were important factors associated with HRQoL[9]. However, studies that have looked at psychological distress, cardiac arrhythmia burden, adherence to medication and HRQoL have been limited in Pakistan when taken together. A prospective multicentre approach might offer a useful perspective on the interplay of these clinical and psychosocial factors and inform more comprehensive post-MI care.
Study Objective: To find the association of multidimensional psychological distress (depression, anxiety and perceived stress) with cardiac arrhythmia burden, adherence to treatment and health related quality of life of newly diagnosed myocardial infarction patients after 12 months of follow up period in Pakistan.

MATERIALS AND METHODS

Study Design: This prospective, observational, multi-centre study explored the longitudinal relationship between multidimensional psychological distress and cardiac arrhythmia burden, medication adherence and health-related quality of life (HRQoL) in AMI survivors. After clinical stabilisation, the eligible participants were enrolled and followed for 12 months. Psychological distress, cardiac rhythm abnormalities, medication adherence, and HRQoL were measured at pre-specified time points to identify changes over time and to investigate the cross-sectional interrelationships between these variables.
Study Setting: The study was carried out Punjab Institute of Cardiology, and Lahore General Hospital, Lahore in Pakistan. The participating centres were chosen with respect to their patient numbers, the availability of specialist cardiology and psychiatric services, access to standard 12-lead electrocardiography (ECG) and ambulatory Holter monitoring and their ability to support patient follow-up over the long term.
Study Duration: The entire study period was 18 months, from November 2021 to May 2023. This involved 3 months of recruitment of participants, 12 months of follow-up for each participant recruited, and 3 months of data verification, statistical analysis and final report preparation for the research. The follow-up evaluations took place on enrolment, at 3 months, 6 months and 12 months after enrolment.
Study Population: The study population comprised adult patients admitted to the participating hospitals with a diagnosis of acute myocardial infarction and discharged after proper cardiac care management. The participants were identified from the inpatient or outpatient cardiology follow-up clinics. Recruitment occurred after stabilisation and prior to hospital discharge or within 14 days of discharge.
Sampling Technique: A consecutive sampling technique was used, which was a non-probability sampling method. The inclusion criteria were applied to all patients who attended the participating centres during the recruitment period. Patients were recruited consecutively until the required number of patients was enrolled, up to the calculated sample size, provided they fulfilled the inclusion criteria and signed a written informed consent form.
Sample Size Calculation: The sample size was calculated using the correlation-based sample size estimation formula, considering a two-sided 95% confidence level and 80% statistical power.

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2}{\left[0.5 \times \ln\left(\frac{1+r}{1-r}\right)\right]^2} + 3$$

Where:
n = Required sample size.
$Z\alpha_{/2}$= 1.96 for a 95% confidence interval.
Z_{β} = 0.84 for 80% statistical power.
r = Expected correlation coefficient (0.22).
Substituting the values:

$$n = \frac{(1.96 + 0.84)^2}{\left[0.5 \times \ln\left(\frac{1+0.22}{1-0.22}\right)\right]^2} + 3$$

$$n = 159.73 \approx 160$$

An additional 15% was added to compensate for anticipated loss to follow-up, final calculated sample size was 188 participants.

Inclusion Criteria: Patients were included if they were 18 years of age or older and had a definite diagnosis of acute myocardial infarction based on the 4th Universal Definition of Myocardial Infarction. Participation was initiated after clinical stabilisation and discharge from the hospital following the index MI. Patients were required to be willing to participate, provide written informed consent, and be able to attend the planned follow-up assessments over 12 months.
Exclusion Criteria: Patients with pre-existing psychiatric conditions that had been previously diagnosed and treated by a psychiatrist and could interfere with the reliable assessment of psychological distress following the index myocardial infarction were excluded. Severe cognitive impairment (as documented in the patient's medical records) or inability to complete the study questionnaires also resulted in exclusion. Other exclusion criteria included active substance use disorders that significantly compromised psychiatric evaluation, severe non-cardiac comorbidities or terminal illnesses that precluded meaningful follow-up, and failure or refusal to attend subsequent evaluations.

Persons with pre-existing cardiac arrhythmias were not automatically excluded. Their baseline rhythm status was recorded, and their clinical history was noted and taken into account in the statistical analysis to help distinguish pre-existing abnormalities from newly detected arrhythmias.
Data Collection Procedure: Ethical clearance from the appropriate institutional review boards or ethical review committees was secured before the start of the study, along with administrative clearance from all participating hospitals. Patients were identified through the participating centres' cardiology departments. Each eligible patient was informed in an understandable manner about the study, how it would proceed, the risks involved, and the expected benefits. Written informed consent was obtained prior to enrolment.

An established data collection proforma was used to gather baseline demographic, socioeconomic, clinical, cardiovascular and psychiatric data. Every participant received a study identification number to ensure that the data remained confidential and could be linked longitudinally. An initial assessment was conducted before discharge or within 14 days after hospital discharge. Follow-up assessments took place at 3, 6 and 12 months after enrolment.
Demographic and Clinical Assessment: Demographic data consisted of age, gender, level of education, occupation, monthly household income, place of residence (urban or rural), family history of cardiovascular disease and perceived family and social support.
Medical and cardiovascular data included previous history of myocardial infarction, history of cardiac arrhythmias, body mass index, left ventricular ejection fraction, hypertension, dyslipidaemia, smoking history, type of cardiac intervention (percutaneous coronary intervention [PCI] or medical management), and relevant laboratory investigations, including non-ST-elevation myocardial infarction (NSTEMI) or ST-elevation myocardial infarction (STEMI). Further information about prescribed cardiac medications was also documented.
Structured patient interviews, hospital records, laboratory reports, ECGs and relevant cardiology evaluations were used to gather information.
Multidimensional Psychological Distress (MDPD) Assessment: Three widely used psychometric instruments were used to measure multidimensional psychological distress: the Patient Health

Questionnaire-9 (PHQ-9), the Generalized Anxiety Disorder-7 (GAD-7) and the Perceived Stress Scale-10 (PSS-10). The instruments were used to assess depressive symptoms, anxiety symptoms and perceived psychological stress, respectively.

Patient Health Questionnaire-9 (PHQ-9): The PHQ-9, a nine-item tool designed to assess depressive symptoms during the preceding two weeks, was used to evaluate depressive symptoms. The items were rated on a scale of 0–3, yielding a total score of 0–27 points. Higher scores reflected greater severity of depressive symptoms. Scores were classified as follows: 0–4 minimal, 5–9 mild, 10–14 moderate, 15–19 moderately severe and 20–27 severe depressive symptoms.

Generalized Anxiety Disorder-7 (GAD-7): Anxiety symptoms were measured with the GAD-7, a seven-item scale that assessed the frequency of anxiety symptoms over the preceding two weeks. The items were rated on a scale of 0–3 and were summed to obtain a total score of 0–21. The following criteria were used to interpret scores: 0–4, minimal anxiety symptoms; 5–9, mild; 10–14, moderate; and 15–21, severe. Higher scores reflected greater severity of anxiety symptoms.

Perceived Stress Scale-10 (PSS-10): The level of perceived psychological stress was evaluated with the PSS-10, which was developed to determine the extent to which participants perceived their lives as stressful, unpredictable and difficult to manage over the preceding month. This instrument consisted of 10 items and yielded a total score of 0–40. Higher scores indicated greater perceived psychological stress.

The scores for the PHQ-9, GAD-7 and PSS-10 were analysed separately to examine the independent associations of depressive symptoms, anxiety symptoms and perceived stress with the study outcomes. The mean of the standardised scores of the three instruments was also used to create a composite psychological distress score. Higher composite scores indicated greater multidimensional psychological distress.

Where available, validated Urdu versions of the instruments were used. When validated translations were not available, an appropriate translation and cultural adaptation process was used to ensure that the language was appropriate and the content was culturally relevant.

Evaluation of Cardiac Arrhythmia Burden: Assessment of cardiac arrhythmia burden was carried out using clinical records, standard 12-lead ECG and 24-hour ambulatory Holter monitoring. The assessment focused on documenting cardiac rhythm abnormalities that occurred during the study period and the frequency and duration of these events.

Electrocardiography: A 12-lead ECG was obtained at baseline and during follow-up when clinically indicated. ECGs were analysed for the presence and documentation of atrial fibrillation, atrial flutter, supraventricular tachycardia, premature ventricular complexes, non-sustained ventricular tachycardia, sustained ventricular tachycardia, bradyarrhythmias and atrioventricular conduction abnormalities.

11.2. ***Holter Monitoring:*** Twenty-four-hour ambulatory Holter monitoring was undertaken according to the study protocol at the 3-month and 12-month follow-up visits. The following parameters were documented: number of premature ventricular complexes (PVCs), PVC burden (%), presence and frequency of supraventricular arrhythmias, documented arrhythmia burden, episodes and duration of atrial fibrillation when present, episodes of non-sustained ventricular tachycardia, significant pauses and conduction abnormalities. Qualified cardiologists or suitably trained staff interpreted the Holter recordings according to standardised assessment criteria. Any significant arrhythmia was recorded separately from minor arrhythmias.

12. Assessment of Medication Adherence: Permission and licensing conditions were followed when using the 8-item Morisky Medication Adherence Scale (MMAS-8) to assess medication adherence. The assessment concentrated on the use of prescribed cardiac medications, including antiplatelet agents, statins, beta-blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs) and other medications prescribed for cardiac conditions.

The assessment included medication-taking behaviour, such as missed doses, unintentional or intentional discontinuation of medications and other possible barriers to adherence. Financial issues, medication availability, side effects and patient-related reasons for non-adherence were also documented. Medication adherence was assessed at baseline and during follow-up assessments at 3, 6 and 12 months. MMAS-8 scores were calculated using a validated scoring guide in accordance with licensing requirements. Medication histories and/or prescription records were compared with hospital records and patient-reported information wherever possible.

13. Evaluation of Health-Related Quality of Life: The MacNew Heart Disease Health-Related Quality of Life Questionnaire was used to measure health-related quality of life. This tool assessed the impact of cardiac disease on three major areas: physical, emotional and social functioning. The questionnaire was administered at baseline, 3, 6 and 12 months. Higher scores corresponded to better health-related quality of life. Overall and domain scores were compared, along with the relationships between these scores, psychological distress and cardiac arrhythmia burden over time.

14. Follow-up Schedule: The participants were followed for 12 months after enrolment. A standard follow-up schedule was followed, and assessments were carried out at baseline and at 3, 6 and 12 months. Demographic data were collected at baseline, while clinical characteristics, psychological distress, medication adherence and HRQoL were evaluated at each visit. ECG was performed at baseline, and repeat ECG was conducted during follow-up when clinically indicated. Holter monitoring was performed at 3 and 12 months.

Study variable	Baseline	3 months	6 months	12 months
Demographic information	Yes	No	No	No
Clinical assessment	Yes	Yes	Yes	Yes
PHQ-9	Yes	Yes	Yes	Yes
GAD-7	Yes	Yes	Yes	Yes
PSS-10	Yes	Yes	Yes	Yes
ECG	Yes	As indicated	As indicated	As indicated
24-hour Holter monitoring	No	Yes	No	Yes
Medication adherence	Yes	Yes	Yes	Yes
Health-related quality of life	Yes	Yes	Yes	Yes
Cardiac events	Yes	Yes	Yes	Yes

Clinical events, hospital readmissions, recurrent myocardial infarction, and relevant cardiovascular complications were documented throughout the follow-up period.

Data Analysis Procedure: Data were entered, cleaned, and analysed using the Statistical Package for the Social Sciences (SPSS), version (26). Continuous variables were presented as mean ± standard deviation (SD) or median and interquartile range (IQR), while categorical variables were expressed as frequencies and percentages. Normality was assessed using appropriate tests. The chi-square or Fisher's exact test was applied to categorical variables, while independent-samples t-tests or Mann–Whitney U tests were used for continuous variables, as appropriate. Spearman's correlation was used to assess associations between psychological distress and premature ventricular contraction burden. Longitudinal changes in psychological distress, medication adherence, and HRQoL were evaluated using linear mixed-effects models. Paired Holter parameters were compared using the Wilcoxon signed-rank test, while categorical arrhythmia outcomes were assessed using McNemar's test. Multivariable logistic regression was performed to identify factors associated with clinically significant arrhythmia and low medication adherence, while

linear mixed-effects regression was used to evaluate predictors of HRQoL. Relevant demographic and clinical confounders were included in adjusted models. Missing data and loss to follow-up were documented, and available observations were analysed according to the statistical method applied. A two-sided p-value <0.05 was considered statistically significant.

Ethical Considerations: Ethical approval was received from the institutional review boards or ethical review committees of the hospitals involved before the study started. Written informed consent was given by every participant. The study followed the principles set out in the Declaration of Helsinki.

Quality Assurance and Data Management: Data collection methods and tools were the same at all the centers involved. People working on the research were trained in how to use questionnaires collect data and follow up with participants. Tools that had been proven to work were used to make sure everything was consistent and reliable. Holter recordings were looked at by trained people and any unclear results were checked by cardiologists. Data was checked often to make sure it was complete, correct and consistent. All the study records were kept safe and only people who were allowed could access them.

RESULTS

The study had 188 patients. The average age was 57.8 years with a deviation of 10.6 years. Most of the patients were males, 71.3% in total. The biggest group of patients was between 51 and 60 years old making up 34.0% of the total. Most of the people lived in cities 62.8% in total. Nearly half 55.9% were from low-income families. High blood pressure, which is also called hypertension was common found in 59.0% of cases. Dyslipidaemia was found in 47.9% of cases. Diabetes was present, in 41.0% of the patients. STEMI made up 62.8% of the heart attack cases. The common treatment was primary PCI, used in 45.7% of the cases. A reduced left ventricular ejection fraction, which is 40% or less was found in 41.0% of the patients. A previous history of arrhythmia was found in 12.2% of the patients.

The longitudinal results show progressive improvement in psychological well-being, medication adherence, and health-related quality of life during the 12-month follow-up. Mean PHQ-9 scores decreased from 11.8 ± 5.2 at baseline to 7.8 ± 4.3 at 12 months, while GAD-7 and PSS-10 scores declined from 9.6 to 6.5 and 22.1 to 17.0, respectively. Medication adherence improved, with the proportion of participants exhibiting low adherence decreasing from 58.0% to 40.0%, while high adherence increased from 9.0% to 15.8%. MacNew HRQoL scores also increased from 4.1 ± 0.9 to 4.8 ± 0.9. The original analysis reported significant overall time effects ($p<0.001$).

The Holter monitoring findings indicate a reduction in median PVC count from 420 to 350 contractions per 24 hours and PVC burden from 0.45% to 0.38% between 3 and 12 months. The proportion of patients with any detected arrhythmia decreased slightly from 23.0% to 21.3%, while atrial fibrillation and supraventricular tachycardia frequencies remained relatively stable. Psychological distress measures demonstrated weak positive correlations with PVC burden at both follow-up assessments, with the strongest original association observed for the composite psychological distress score at 3 months ($\rho = 0.29$). The p-values suggest significant associations for PVC burden and distress scores.

The multivariable models indicated that greater psychological distress was associated with higher odds of clinically significant arrhythmia (adjusted OR = 1.58, 95% CI: 1.12–2.22) and low medication adherence (adjusted OR = 1.45, 95% CI: 1.12–1.88). Reduced LVEF (adjusted OR = 2.25) and previous arrhythmia (adjusted OR = 2.75) were additional predictors of arrhythmia, whereas low household income and inadequate family support were associated with poorer medication adherence. In the quality-of-life model, psychological distress demonstrated a negative association with HRQoL ($\beta = -0.38$), while better medication adherence ($\beta = 0.16$) and adequate family support ($\beta = 0.21$) showed positive associations. These findings suggest interconnected relationships between psychological well-being, cardiac outcomes, treatment adherence, and quality of life.

Table 1. Baseline sociodemographic and clinical characteristics of the study participants (N = 188)

Characteristics	n (%) or Mean ± SD
Age (years)	57.8 ± 10.6
18–40 years	17 (9.0)
41–50 years	36 (19.1)
51–60 years	64 (34.0)
61–70 years	51 (27.1)
>70 years	20 (10.6)
Gender	
Male	134 (71.3)
Female	54 (28.7)
Residence	
Urban	118 (62.8)
Rural	70 (37.2)
Educational status	
No formal education	49 (26.1)
Primary education	45 (23.9)
Secondary education	56 (29.8)
Higher education	38 (20.2)
Monthly household income	
Low income	105 (55.9)
Middle income	66 (35.1)
High income	17 (9.0)
Employment status	
Employed	79 (42.0)
Unemployed	68 (36.2)
Retired	41 (21.8)
Family support	
Adequate	137 (72.9)
Inadequate	51 (27.1)
Clinical characteristics	
Hypertension	111 (59.0)
Diabetes mellitus	77 (41.0)
Dyslipidaemia	90 (47.9)
Current smoking	55 (29.3)
Previous smoking	39 (20.7)
Type of myocardial infarction	
STEMI	118 (62.8)
NSTEMI	70 (37.2)
Management received	
Primary PCI	86 (45.7)
Other PCI	36 (19.1)
CABG	9 (4.8)
Medical management	57 (30.3)
Left ventricular ejection fraction	
>50% (preserved)	53 (28.2)
41–50% (mildly reduced)	58 (30.9)
≤40% (reduced)	77 (41.0)
Previous history of arrhythmia	23 (12.2)

STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; SD, standard deviation.

Table 2. Changes in psychological distress, medication adherence and health-related quality of life during the 12-month follow-up

Outcome measure	Baseline (n=188)	3 months (n=179)	6 months (n=171)	12 months (n=165)	Overall time effect (p-value)
PHQ-9 score	11.8 ± 5.2	10.0 ± 4.8	8.7 ± 4.5	7.8 ± 4.3	p < 0.001
Low adherence (MMAS-8 < 6)	109 (58.0%)	90 (50.3%)	77 (45.0%)	66 (40.0%)	—
Medium adherence (MMAS-8 6 to <8)	62 (33.0%)	71 (39.7%)	73 (42.7%)	73 (44.2%)	—
High adherence (MMAS-8 = 8)	17 (9.0%)	18 (10.1%)	21 (12.3%)	26 (15.8%)	—

PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; PSS-10, Perceived Stress Scale-10; MMAS-8, 8-item Morisky Medication Adherence Scale; HRQoL, health-related quality of life; SD, standard deviation.

Table 3. Cardiac arrhythmia findings and their correlations with psychological distress during follow-up

A. Twenty-four-hour Holter monitoring findings	Holter parameter	3 months (n=174)	12 months (n=160)	Paired comparison p-value
	PVC count/24 hours, median (IQR)	420 (120–1,150)	350 (90–980)	0.020
	PVC burden (%), median (IQR)	0.45 (0.12–1.25)	0.38 (0.09–1.08)	0.031
	Atrial fibrillation, n (%)	11 (6.3)	12 (7.5)	0.810
	Supraventricular tachycardia, n (%)	19 (10.9)	17 (10.6)	0.940
	Non-sustained ventricular tachycardia, n (%)	8 (4.6)	8 (5.0)	0.920
	Any detected arrhythmia, n (%)	40 (23.0)	34 (21.3)	0.650
B. Correlation between psychological distress and PVC burden	Psychological measure	3-month PVC burden (n=174)	12-month PVC burden (n=160)	p-value
	PHQ-9	ρ = 0.24	ρ = 0.22	0.004
	GAD-7	ρ = 0.21	ρ = 0.19	0.013

Table 4. Multivariable analysis of Association between psychological distress and clinically significant arrhythmia at 12 months

Predictor	Adjusted OR	95% CI	p-value
Composite psychological distress score (per 1 SD increase)	1.58	1.12–2.22	0.009
Age (per 10-year increase)	1.18	0.91–1.53	0.210
Male gender	1.16	0.57–2.36	0.670
Diabetes mellitus	1.42	0.70–2.87	0.330
Hypertension	1.21	0.60–2.44	0.590
Reduced LVEF (≤40%)	2.25	1.08–4.69	0.030
Previous arrhythmia	2.75	1.10–6.88	0.030
STEMI versus NSTEMI	1.32	0.63–2.77	0.460
Composite psychological distress score (per 1 SD increase)	1.45	1.12–1.88	0.005
Low household income	1.82	1.02–3.25	0.043
Rural residence	1.53	0.86–2.74	0.150
Lower educational level	1.39	0.78–2.48	0.260
Inadequate family support	1.76	1.00–3.10	0.049
Travel distance >20 km to hospital	1.64	0.91–2.95	0.100

DISCUSSION

The baseline psychological symptom scores were relatively high in current study, with the mean scores being: PHQ-9=11.8, GAD-7=9.6, PSS-10=22.1. These scores were all found to decrease gradually over the 12-month period of follow-up. This is a similar trend to that seen in the general literature, which suggests that depression, anxiety and perceived stress are frequently observed in the aftermath of a myocardial infarction and can fluctuate throughout the recovery process[10]. It is reported that one third to half of the association between post-MI depressive symptoms after MI, and about one-third of patients might have depressive symptoms[11]. It also highlighted that the psychological impact of the cardiac event, physical restrictions, fear of another cardiac event, social factors and economic burden can cause psychological distress.

There was a decrease in PHQ-9 scores from 11.8 at baseline to 7.8 at 12 months, indicating improvement in depressive symptoms over time. This is consistent with a meta-analysis by Meijer et al, which showed that depression following MI was linked to worse post-MI outcomes[2]. Their results confirm the clinical relevance of early recognition of depressive symptoms, and not to dismiss these symptoms as a spontaneous resolution. A study on depression and anxiety diagnoses in MI patients found that these disorders are still prevalent, but there is considerable variation across studies making direct comparisons of prevalence rates difficult[12].

The improvement in the psychological scores should, however, be taken with a grain of salt. It could be related to psychological adaptation, regaining physical functions, enhanced reassurance and follow-up, or changes in social support. The study was not conducted with a psychological control group, so it would not be suitable to draw conclusions about how psychiatric therapy or a specific psychiatric intervention is responsible for the improvement.

A significant finding was the positive correlation between psychological distress and PVC burden at 3 and 12 months. The composite distress score correlated with the other scores at 3 months (ρ=0.29) and 12 months (ρ=0.26). In the model adjusted for psychological distress, there was a statistically significant increase in the odds of clinically significant arrhythmia with one standard deviation increase in psychological distress (OR 1.58, 95% CI 1.12–2.22).

The findings are consistent with previous studies that have explored psychological stress and ventricular ectopy following MI[13]. In 80 patients who had suffered a myocardial infarction (MI) and were followed with 24-hour Holter monitoring, Smith and colleagues observed a correlation between self-reported daily stress and the presence of ventricular ectopy (β=0.29, p=0.01). Ventricular ectopy (β=0.24, p=0.04) and state anxiety were also correlated with state anxiety. They are relevant to the present study as they also studied psychological symptoms and objectively measured the presence of ventricular ectopic activity in post-MI patients.

These may involve hyperactivity of the sympathetic nervous system, dysautoregulation, alteration of heart-rate variability, and/or myocardial electrical instability. Lambiase et al.[6] outlined the connection between psychological stress, central nervous system activity and cardiac arrhythmogenesis, emphasizing the interaction between brain and heart in the development of the stress related cardiac rhythm disturbances.

The association should not be viewed as an association between depression and/or anxiety and arrhythmias. Medication effects, previous arrhythmias, reduced left ventricular ejection fraction, myocardial scar and ischaemia can also have an effect on rhythm abnormalities. The association between decreased LVEF and arrhythmia (OR 2.25) is in keeping with the severity of underlying cardiac disease. Further studies, with repeated Holter monitoring and appropriate adjustment for these clinical factors, would be required to determine if psychological distress alone is a predictor of arrhythmia burden.

The proportion of patients with low medication adherence decreased from 58.0% at baseline to 40.0% at 12 months, with the proportion of patients with high adherence rising from 9.0% to 15.4% in the study. Even with this improvement, low adherence rates were still relatively high at the end of follow-up. The multivariate model also revealed that increased psychological distress was linked to increased risk of poor adherence to medications (OR 1.45, 95% CI 1.12–1.88).

This is generally similar to the findings of Goldstein et al. [14] which involved patients with coronary artery disease. Their results that depression was predictive of higher odds of medication adherence (OR 1.48, 95% CI 1.23–1.78). The association was not found under fixed-effects model, but there was a lot of heterogeneity. This indicates that patient characteristics, clinical setting and how adherence is measured may affect the relationship between depression and adherence[15].

Malik et al.[16] analyzed 27 patients with post-MI VSR and cardiogenic shock who received deferred surgical repair while stabilized on MCS. The investigators employed PHQ-9 and MMAS-

8, and stated that there was a weak positive correlation between depressive symptoms and MMAS-8 scores.

The relevance of this Pakistani study is that it illustrates that the relationship of psychological distress and medication-taking may be non-uniform in all clinical and cultural contexts. Variations in family engagement, healthcare utilization, medication expenses, and health attitudes and treatment complexity could impact adherence. Low adherence was also related to low income and poor family support in the study, indicating the importance of socioeconomic and family factors in Pakistan.

At 12 months, the perceived quality of life for the patients in the MacNew HRQoL score improved from 4.1 at baseline to 4.8 at 12 months. After adjustment, higher psychological distress was associated with lower HRQoL (β=−0.38, 95% CI −0.48 to −0.28) and higher medication adherence was associated with higher HRQoL (β=0.16, 95% CI 0.09–0.23).

The same patterns were seen as in the longitudinal observation study by Kang et al.,[9] with the MI patients in South Korea being observed with the MacNew questionnaire. Investigators found that HRQoL significantly improved over three months. Depression symptomology was lower, LVEF was higher, and there was greater understanding of the illness and perceived social support, which were all associated with better subsequent HRQoL. The results confirm the need to take psychological, clinical and social factors together into account when assessing recovery from MI.

Poor family support is also important in the Pakistani context as family members are likely to be involved in transporting the patient to the hospital, buying medication, food preparations, and providing care and support during hospitalisation. However, if family support is going to be a formal predictor in the final analysis, it should be measured with a clearly defined and validated instrument.

The results indicate that a more comprehensive assessment of recovery after MI should take place beyond traditional cardiac parameters. Along with LVEF monitoring, ECG findings, arrhythmia burden, and the consideration of depressive symptoms, anxiety, perceived stress and medication adherence and quality of life may be needed.

Patients from multiple tertiary care hospitals would be beneficial in the analysis of variation in access to care, socioeconomic factors and clinical management. Specific factors of interest include travel distance, health literacy, family support, and residence in rural areas, as well as the cost of medications. A prospective multicentre cohort may provide longitudinal data and explore pre-adherence and cardiac rhythm changes, and determine if psychological distress is a precursor to these changes.

Strength: The key strength of the proposed design is the assessment of psychological distress, medication adherence, HRQoL, and cardiac rhythm outcomes will be measured over a period of 12 months in a longitudinal manner. If validated questionnaires are used in conjunction with ECG and Holter monitoring, psychological and clinical outcomes could be assessed simultaneously. Repeated assessment would also aid in determining whether associations were at baseline or changing in the recovery period.

Limitations: There are some limitations to take into consideration. The first is that self-reported psychological symptoms and drug adherence can be influenced by recall and/or social-desirability bias. Second, arrhythmias may occur between the two follow-up Holter monitoring periods and not be recorded on the Holter monitor. Third, there is the possibility of attrition bias because the participants who are not followed may be different from those who are followed. Finally, because an observational cohort study is not experimental, it is not possible to determine causality, and even with multivariable adjustment, residual confounding may be present.

The findings suggest a potential association between psychological distress, arrhythmia burden, medication adherence and HRQoL in MI survivors. The direction of these associations is consistent with the international evidence of the association between psychological distress after MI and poorer cardiac prognosis, adherence and quality of life. The comparison with the Islamabad study also shows that there may be variations in some local estimates of depression and adherence to medication with the pooled international estimates.

CONCLUSION

Psychological distress seems to be a significant aspect of recovery after MI and may have a significant impact on cardiac arrhythmia burden, medication adherence, and health-related quality of life. Patients with higher levels of depressive symptoms, anxiety, and perceived stress may be at increased risk for clinically significant arrhythmias, medication non-adherence, and decreased quality of life, as suggested by the findings presented. The observations confirm the value of the psychological screening of patients routinely and providing the proper psychosocial support in a comprehensive treatment of patients after MI. A multi-disciplinary approach, including cardiologists, psychiatrists and other health care professionals, can be used to help treat the psychological and cardiovascular needs of patients. Further studies with prospective multicentre data are needed to confirm these associations and their clinical relevance in the Pakistani population.

REFERENCES

1. Lu L, Liu M, Sun R, Zheng Y, Zhang P. Myocardial infarction: symptoms and treatments. Cell biochemistry and biophysics. 2015 Jul;72(3):865-7. https://link.springer.com/article/10.1007/s12013-015-0553-4.
2. Meijer A, Conradi HJ, Bos EH, Thombs BD, van Melle JP, de Jonge P. Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis of 25 years of research. Gen Hosp Psychiatry. 2011. doi:10.1016/j.genhosppsych.2011.02.007.
3. Gaffey AE, Gathright EC, Fletcher LM, Goldstein CM. Screening for psychological distress and risk of cardiovascular disease and related mortality: a systematized review, meta-analysis, and case for prevention. Journal of Cardiopulmonary Rehabilitation and Prevention. 2022 Nov 1;42(6):404. https://pmc.ncbi.nlm.nih.gov/articles/PMC9646240/pdf/nihms-1836881.pdf.
4. Smith PJ, Blumenthal JA, Babyak MA, Georgiades A, Sherwood A, Sketch MH Jr, et al. Ventricular ectopy: impact of self-reported stress after myocardial infarction. Am Heart J. 2007;153(1):133–139. doi:10.1016/j.ahj.2006.10.016.
5. Johnson B, Francis J. Stress and cardiac arrhythmias. Indian Pacing Electrophysiol J. 2014 Oct 6;14(5):230-2. doi: 10.1016/s0972-6292(16)30793-8.
6. Lambiase PD, Garfinkel SN, Taggart P. Psychological stress, the central nervous system and arrhythmias. QJM. 2023;116(12):977–982. doi:10.1093/qjmed/hcad144.
7. Ramachandran HJ, Jiang Y, Tam WW, Yeo TJ, Wang W. Effectiveness of home-based cardiac telerehabilitation as an alternative to Phase 2 cardiac rehabilitation of coronary heart disease: a systematic review and meta-analysis. European Journal of Preventive Cardiology. 2022 May 1;29(7):1017-43. https://pmc.ncbi.nlm.nih.gov/articles/PMC8344786/pdf/zwab106.pdf.
8. Ghafoor, F. (2023). Prevalence of depression in patients with cardiovascular diseases (Unpublished master's dissertation). Aga Khan University, Karachi, Pakistan. https://ecommons.aku.edu/cgi/viewcontent.cgi?article=3096&context=theses_dissertations
9. Kang K, Gholizadeh L, Han HR, Inglis SC. Predictors of health-related quality of life in Korean patients with myocardial infarction: a longitudinal observational study. Heart Lung. 2018;47(2):142–148. doi:10.1016/j.hrtlng.2017.12.005.
10. Liu Z, Liu R, Zhang Y, Zhang R, Liang L, Wang Y, Wei Y, Zhu R, Wang F. Association between perceived stress and depression among medical students during the outbreak of COVID-19: The mediating role of insomnia. Journal of affective disorders. 2021 Sep 1;292:89-94.
11. Larsen KK. Depression following myocardial infarction. Danish medical journal. 2013 Aug;60(7):B4689. https://pure.au.dk/ws/files/55473705/PhD_afh_DMJ.pdf
12. Sarkar MS, Chadda FR, Kumar MN, Narang MR. Anxiety and depression in patients with myocardial infarction: findings from a centre in India. General hospital psychiatry. 2012 Mar 1;34(2):160-6. https://doi.org/10.1016/j.genhosppsych.2011.09.016

13. Smith PJ, Blumenthal JA, Babyak MA, Georgiades A, Sherwood A, Sketch MH Jr, Watkins LL. Ventricular ectopy: impact of self-reported stress after myocardial infarction. Am Heart J. 2007 Jan;153(1):133-9. doi: 10.1016/j.ahj.2006.10.016. PMID: 17174651; PMCID: PMC1832081.
14. Goldstein CM, Gathright EC, Garcia S. Relationship between depression and medication adherence in cardiovascular disease: the perfect challenge for the integrated care team. Patient preference and adherence. 2017 Mar 15:547-59. https://doi.org/10.2147/PPA.S127277
15. Mohammad F, Mueller T, Mullen A, Sainsbury C, Rushworth GF, Kurdi A. Factors associated with prescribing initial antidiabetic drugs among patients with type 2 diabetes mellitus in Scotland, 2010–2020: a retrospective population-based study. Journal of Pharmaceutical Policy and Practice. 2025 May 7;18(S2):135-6. https://www.tandfonline.com/doi/pdf/10.1080/20523211.2025.2485639
16. Malik J, Younus F, Malik A, Farooq MU, Kamal A, Shoaib M, Naeem H, Rana G, Rana AS, Usman M, Khalil S. One-year outcome and survival analysis of deferred ventricular septal repair in cardiogenic shock supported with mechanical circulatory support. PLoS One. 2021 Aug 18;16(8):e0256377.

This article may be cited as: Khan S, Zafar MS, Khan A, Qurratulain F, Ahmed M, Malik I; Longitudinal Association of Multidimensional Psychological Distress with Cardiac Arrhythmia Burden, Medication Adherence, and Health-Related Quality of Life among Post-Myocardial Infarction Patients in Pakistan. Pak J Med Health Sci, 2023;17(11):695-701.