

The prevalence of medication nonadherence in post-myocardial infarction survivors and its perceived barriers and psychological correlates: a cross-sectional study in a cardiac health facility in Malaysia

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Background: Although evidence-based practice has shown the benefits of prescribed cardioprotective drugs in post-myocardial infarction (MI) survivors, adherence rates remain suboptimal. The aim of this study was to determine the prevalence and factors associated with medication nonadherence among post-MI survivors in Malaysia.

Materials and methods: This cross-sectional study was conducted from February to September 2016 among 242 post-MI survivors aged 24–96 years at the cardiology outpatient clinic in a Malaysian cardiac specialist center. The study utilized an interviewer-administered questionnaire that consisted of items adapted and modified from the validated Simplified Medication Adherence Questionnaire, sociodemographics, health factors, perceived barriers, and novel psychological attributes, which employed the modified Confusion, Hubbub, and Order Scale and the Verbal Denial in Myocardial Infarction questionnaire.

Results: The prevalence of medication nonadherence was 74%. In the multivariable model, denial of illness (AOR 1.2, 95% CI 0.9–1.8; $P=0.032$), preference to traditional medicine (AOR 8.7, 95% CI 1.1–31.7; $P=0.044$), lack of information about illness (AOR 3.3, 95% CI 1.1–10.6; $P=0.045$), fear of side effects (AOR 6.4, 95% CI 2.5–16.6; $P<0.001$), and complex regimen (AOR 5.2, 95% CI 1.9–14.2; $P=0.001$) were statistically significant variables associated with medication nonadherence.

Conclusion: The relatively higher medication-nonadherence rate in this study was associated with patient-, provider-, and therapy-related factors and the novel psychological attribute denial of illness. Future research should explore these factors using robust methodological techniques to determine temporality among these factors.

Keywords: medication nonadherence, myocardial infarction, perceived barriers, psychology

Background

Evidence-based practice has shown the benefits of prescribed cardioprotective drugs in post-myocardial infarction (MI) survivors.¹ Despite proven efficacy, adherence rates remain suboptimal, ranging 40%–70% globally.^{2,3} Asian countries report higher medication-nonadherence rates, 40%–80%,⁴ while in Malaysia the medication-nonadherence rate in post-MI patients averages 50%.⁵ This relatively poor adherence to medication has predisposed patients to greater clinical complications, recurrent hospital admissions, increased mortality, and escalated health-care expenditure.^{6,7}

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The World Health Organization (WHO) defines “adherence” as “the extent to which a person’s behavior – taking medications, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider”.⁸ Established correlates of medication nonadherence include demographic factors,^{9,10} socioeconomic factors like health coverage,¹¹ and disease comorbidities.^{10,11} Doctor’s prescriptions and follow-up plans are often challenged when patients launch a series of justifications for not wanting to adhere, including cost, accessibility, nuisance, potential side effects, lack of knowledge of current health condition, preference for traditional medicines, and a complex regimen.^{12–16} Other reasons for lack of adherence to medications include poor communication, poor rapport with health-care providers, and a lack of continuity in care.^{13,15,17}

Recent literature has hypothesized potential psychological factors to influence medication nonadherence. One such psychological factor postulated to influence medication adherence is life chaos.¹⁵ Chaotic lifestyles and environment encompass myriad factors, including variability in daily routines, ability to plan and anticipate the future, punctuality, ability to maintain financial stability, employment, housing, and ability to maintain appointments.¹⁵ Two recent preliminary investigations from the US found an association of life chaos with medication nonadherence among post-MI survivors.^{15,18}

There are conflicting reports on the influence of denial of medication nonadherence. Some argued that denial is associated with faster recovery, better psychosocial readjustment, and lower mortality, but evidence for these claims is potentially confounded by many medical, psychological, and social factors.^{19–23} One study that explored post-MI coping experiences through a grounded-theory approach postulated that it was not easy to integrate treatment-related behavior patterns into one’s everyday life or to give up old habits, as the need for change is influenced by both behavioral and psychosocial factors.²⁴ The influence of MI on patients depends on their perception of the illness and coping abilities. Kentsch et al reported that a quarter of patients in their study overtly said that they did not want to acknowledge their symptoms, admitting that they used denial as a coping strategy.²⁵ This coping strategy appears to be related to delayed treatment-seeking behavior, because they wait for symptoms to go away and they do not take post-MI care seriously, not wanting to bother anybody, and they tend to self-medicate.²² No published studies have investigated the association of denial and medication nonadherence in post-MI patients.

The health-belief model postulates that patient engagement in health-related behaviors like medication adherence

is often influenced by various “modifying factors”. These factors determine how patients perceive the threat of their health problems, which subsequently determines their likelihood to adhere to agreed treatment recommendations. Previous evidence has largely been derived from national health registries, clinical data repositories, and administrative data sets. These revealed limited information about certain types of modifying factors related to individual psychology or behavior, knowledge deficits, and self-beliefs that influence medication taking. To address the existing gap, this study aims to evaluate associations among perceived barriers, established correlates, and new psychological factors with medication nonadherence among post-MI survivors in Malaysia.

Materials and methods

Study setting and population

This cross-sectional single-center study was conducted from February to September 2016 among post-MI patients who were on follow-up at the Cardiology Outpatient Department of Serdang Hospital, Selangor, Malaysia. Serdang Hospital is one of the three premier cardiac centers in Malaysia, along with the National Heart Institute in Kuala Lumpur and Sarawak General Hospital in Borneo. The hospital is the main cardiac center in Selangor, one of the 14 states in Malaysia, and coupled with the National Heart Institute they share an equal burden for cardiac referral cases throughout Peninsular Malaysia.²⁶ Eligibility for sample recruitment included MI survivors prescribed post-MI treatment regimen that included antiplatelets, statins, anti-ischemic agents like β -blockers, ACE inhibitors, or angiotensin-receptor blockers, as documented by a physician based on the diagnostic criteria of the Malaysian clinical practice guidelines.²⁷ Patients had to be aged 18 years or older and discharged from the hospital at least 1 month post-MI. Patients were excluded if they had multiple significant comorbidities likely to cause mortality, such as a combination of disease clusters in addition to the diagnosis of MI (hypertension, diabetes, and heart failure; hypertension, diabetes, and stroke; cardiac arrhythmias; or other acquired cardiac illness or terminal illnesses that do not share common risk factors or pathogenic pathways of MI) that were evidenced to have greater odds of dying,²⁸ diagnosed with stable or unstable angina, cognitively impaired, or with an active mental illness.

Sample size

Based on a sample-size calculation for a study of finite population,²⁹ with roughly 500 post-MI survivors from Serdang

Hospital,³⁰ a sample size of 217 patients was calculated to represent a cross-section of the population and to allow the study to determine the prevalence of medication nonadherence with a margin of error of $\pm 5\%$.³¹ An additional 20% were included in the calculated sample³² to compensate for possible missing data or nonresponse, for a final sample size of 261.

Ethics statement

This study complied with the guidelines covered in the Declaration of Helsinki. Ethical approval was obtained from the Medical Research Ethics Committee, Ministry of Health Malaysia (government approval NMRR-15-2210-28696-IIR). The study objectives and benefits were explained verbally and documented in a form attached to the questionnaires. Respondents' confidentiality and anonymity was assured. Written consent was obtained from those who agreed to participate.

Study instruments

Data for this study were collected using an interviewer-assisted questionnaire comprised of five parts, while clinical health information was derived from patient medical records. The first part consisted of sociodemographic information (sex, age-group, marital status, education level, monthly household income, employment status, and residence-hospital distance). Age and marital status were categorized according to current population estimates for Malaysia.³³ Income level was categorized according to Malaysia's 2014 median household income and basic amenities survey.³⁴

In the second part, the respondent's self-rated general health status was measured using the single validated item, "How would you rate your current health status?", with five response alternatives: poor (5), fair (4), good (3), very good (2), and excellent (1).³⁵ These items were reversed and categorized as good (1–3) and poor (4–5), consistent with previous reported scoring rules.^{36,37}

The primary outcome measure, medication nonadherence, was evaluated in the third part. The authors adapted and modified items from the validated six-item Simplified Medication Adherence Questionnaire (SMAQ), developed by Knobel et al.³⁸ The modified SMAQ utilized in this study was intended to measure medication nonadherence for all prescribed medications based on the Malaysian clinical practice guidelines for a post-MI treatment regimen. Two items intended to measure frequency of medication nonadherence in the original scale were excluded. The modified SMAQ that measured nonadherence using four items in the current study identified two main subtypes of nonadherence: unintentional nonadherence (when patients wish to adhere to medication,

but are prevented from taking it for some reason; based on forgetfulness and clarification regarding the medical regimen) and intentional nonadherence (when patients deliberately do not take their medications; based on withdrawing medications when feeling better or worse).^{39,40} Items in the adapted and modified SMAQ scale included: Do you ever forget to take your medicine?; Are you careless at times about taking your medicine?; Sometimes if you feel worse, do you stop taking your medicines?; and Did you decide to self-omit or alter prescribed doses of your medications? As the SMAQ was dichotomous, any answer in the sense of nonadherent was considered nonadherent.³⁸ The four-item scale had a scoring scheme of yes = 1 and no = 0. The items were summed to give a range of scores of 0–4. Total scores were dichotomized, with a score of 0 as adherent and scores of 1–4 as nonadherent.

The fourth part explored barriers to medication taking. Three domains with five items in accordance with the WHO framework of medication adherence⁸ were evaluated: patient factors (prefer taking traditional medicine, lack of transportation),¹⁶ provider or health-system factor (lack of information about illness),¹⁶ and therapeutic factors (complex regimen, fear of side effects)¹³ using validated single-item reported measures adapted from previous studies. Respondents were asked, "Thinking of your current cardiac health situation, what would be the possible barriers for you for not wanting to take prescribed medications?" Respondents were given the response option of yes = 1 or no = 0.

Psychological factors were assessed in the fifth part. Perceived life chaos was explored through the validated six item of the Malay version of the Confusion, Hubbub, and Order Scale (CHAOS-6).⁴¹ This scale was designed to evaluate chaos in one's life that addressed consistency of daily routine, ability to plan and anticipate future activities, and being on time.^{15,42,43} This six-item scale constituted the following items: "My life is organized", "My life is unstable", "My routine is the same from week to week", "My daily activities from week to week are unpredictable", "Keeping a schedule is difficult for me", and "I don't like to make appointments too far in advance because I don't know what might come up." Response choices were recorded on a 5-point Likert scale ranging from "definitely true" to "definitely false." Scoring of the CHAOS scale was performed by summing item responses and ranged 6–30, such that a higher score indicated a more chaotic lifestyle.^{15,18}

Subsequently, respondent acceptance of cardiac illness was measured using the validated eight-item Verbal Denial in Myocardial Infarction questionnaire.²⁰ This scale encompasses three domains: denial of illness (two items), denial of impact (four items), and suppression (two items).

These scale items were rated on a 5-point Likert scale ranging from “disagree completely” to “agree completely”. Scoring of the total scale and the three subscales was performed by summing the item responses such that higher scores indicated a greater denial of MI.²⁰

Clinical health information, such as time from MI event and disease comorbidities (diabetes, hypertension, or hypercholesterolemia), were derived from patient records. Baseline parameters are defined as follows: patients with fasting plasma glucose level 7 mmol/L (126 mg/dL) or above and prescribed oral hypoglycemic agents or insulin regimen, as documented in medical records, were classified as having diabetes;⁴⁴ patients were labeled hypertensive if they had been previously diagnosed with hypertension and administered antihypertensives, as documented in medical records;⁴⁴ hypercholesterolemia was defined as total cholesterol more than 5.2 mmol/L with high plasma triglyceride concentration (>1.7 mmol/L), low high-density-lipoprotein cholesterol concentration (<1 mmol/L for men, <1.3 mmol/L for women), and increased concentration of low-density-lipoprotein cholesterol (>2.6 mmol/L with cardiac risk factors) with patients currently on statins, as documented in medical records.⁴⁵ Table 1 briefly describes the study instrument.

Statistical analyses

Analysis was conducted using STATA version 13.0 (StataCorp, College Station, TX, USA). To check the validity of the modified SMAQ among the Malaysian population, an exploratory factor analysis was performed using principal-component analysis by the direct oblimin method. The Kuder–Richardson test was performed to test the internal consistency and reliability of the modified SMAQ binary-measure scale in this study sample. Cronbach’s α -value for the Verbal Denial of Myocardial Infarction scale was also used to test the internal consistency of the scale. Descriptive statistics

were obtained for all variables in the study. Cross-tabulation analysis was used to obtain the proportions. Simple logistic regression analysis was used to obtain ORs and to assess the association between medication nonadherence and categorical variables. Multiple logistic regression analysis using stepwise backward elimination was performed to obtain the final model and AORs. All independent variables with significant associations in the univariate analyses were included in the multivariate analysis. The significance level was set to 0.05 ($P < 0.05$).

Results

Sample characteristics

A total of 261 consecutive patients were invited to participate in the study, and 242 (92.7% response rate) participated. The sample constituted 208 (85.9%) men and 34 (14.1%) women. The mean (\pm SD) age of the respondents was 55 (\pm 11) years, with a range of 24–96 years. Most respondents were married (85.9%), had attained secondary education or less (90.1%), and employed (62.8%), with a monthly household income of less than RM4,500 (US\$1 = RM4.40) (89.4%). The mean (\pm SD) of residence–hospital distance was 26.8 (\pm 33.7) km, and the distance ranged 1–250 km (Table 2). The mean (\pm SD) time from MI event was 22 (\pm 24.5), range 1–204 months. The bulk of respondents perceived themselves to have “good” health status (73.1%). With regard to disease comorbidities, 67.8% of the respondents had hypertension, 62.8% hypercholesterolemia, and 47.5% diabetes (Table 2).

Medication nonadherence and perceived barriers

Exploratory factor analyses using the direct oblimin method of the modified SMAQ yielded one factor with given eigenvalue greater than 1 (2.9). The one-factor solution accounted for 51% of the variance. Factor loading ranged from 0.67 to 0.8.

Table 1 Summary of the study instrument

Subsection	Content	Mode of data collection
Sociodemographics	Sex, age-group, marital status, education level, monthly household income, employment status, residence–hospital distance	Questionnaire
General health status	Single validated item – “How would you rate your current health status?” – with five response alternatives: poor (5), fair (4), good (3), very good (2), excellent (1)	Questionnaire
Medication nonadherence	Modified four-item Simplified Medication Adherence Questionnaire	Questionnaire
Barriers to medication taking	Five single-item reported measures adapted from previous literature in accordance with WHO Framework of Medication Adherence	Questionnaire
Psychological factors (perceived life chaos and acceptance of cardiac illness)	Validated six-item modified Confusion, Hubbub, and Order Scale and eight-item Verbal Denial in Myocardial Infarction questionnaire	Questionnaire
Clinical health information	Time from MI event, comorbidities: diabetes, hypertension, and hypercholesterolemia	Patient medical records

Abbreviations: MI, myocardial infarction; WHO, World Health Organization.

Table 2 Sociodemographics and health attributes of respondents (n=242)

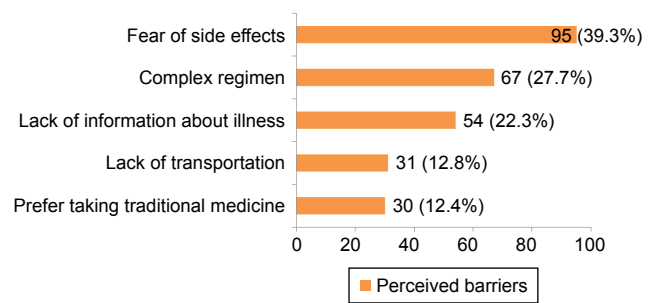
Characteristics	n (%)
Sex	
Women	34 (14.1)
Men	208 (85.9)
Age-group (years)	
≥60	86 (35.5)
18–59	156 (64.5)
Mean ± SD	55±11
Marital status	
Married	208 (85.9)
Single	34 (14.1)
Education level	
Tertiary education	24 (9.9)
Secondary education or less	218 (90.1)
Monthly household-income level (RM, n=236)	
≥4,500	25 (10.6)
<4,500	211 (89.4)
Employment status following MI	
Not working	90 (37.2)
Working	152 (62.8)
Perceived current health status	
Good	177 (73.1)
Poor	65 (26.9)
Diabetes	
No	127 (52.5)
Yes	115 (47.5)
Hypertension	
No	78 (32.2)
Yes	164 (67.8)
Hypercholesterolemia	
No	90 (37.2)
Yes	152 (62.8)
Time from MI event (months), mean ± SD	22±24.5
Residence–hospital distance (km), mean ± SD	26.8±33.7

Abbreviation: MI, myocardial infarction.

The Kuder–Richardson internal consistency and reliability test for the binary measure of the modified-SMAQ scale was 0.65, suggesting acceptable internal consistency for the study sample. The prevalence of medication nonadherence in this study was 74%. Reasons cited included fear of side effects (39.3%), complex regimen (27.7%), lack of information about illness (22.3%), lack of transport (12.8%), and preference for traditional medicine (12.4%) (Figure 1).

Psychological attributes

Cronbach's α -coefficient for the Verbal Denial in Myocardial Infarction Questionnaire was 0.62, suggesting acceptable internal consistency suitable for the Malaysian population. The mean (\pm SD) perceived life-chaos score was 15 (\pm 5.3), ranging 6–30. The mean (\pm SD) denial-of-illness score was 4.5 (\pm 2.5), and the total sub-domain score ranged 2 to 10. The mean (\pm SD) denial of impact score was 10.7 (\pm 4), and

**Figure 1** Perceived barriers to taking medication.

the total subdomain score ranged 4–20. The mean (\pm SD) suppression score was 6.9 (\pm 2.6), ranging 2–10. The mean (\pm SD) of the total cardiac denial sum score was 22.1 (\pm 6.2), ranging 8–37.

Association of sociodemographic and health-related factors with medication nonadherence

Men had about threefold the odds of women of nonadherence to medications (OR 2.6, 95% CI 1.2–5.6; $P=0.01$). Similarly, patients aged 18–59 years had about double the odds of those aged ≥ 60 years of nonadherence to medications (OR 1.8, 95% CI 1.1–3.3; $P=0.01$). Patients with hypercholesterolemia had double the odds of those without hypercholesterolemia of nonadherence to medications (OR 2, 95% CI 1.1–3.5; $P=0.022$). A 1-month increase in time from the MI event was associated with a 10% increase in the odds of medication nonadherence (OR 1.1, 95% CI 0.9–1.2; $P=0.041$). A 1 km increase in distance between residence and hospital was associated with a 10% increase in the odds of medication nonadherence (OR 1.1, 95% CI 0.9–1.2; $P=0.045$) (Table 3).

Association between psychological attributes and medication nonadherence

Table 4 exhibits the associations between the psychological attributes and medication nonadherence. A 1-unit increase in life-chaos score was associated with a 10% increase in the odds of being nonadherent to medications (OR 1.1, 95% CI 0.9–1.2; $P=0.003$). A 1-unit increase in the denial-of-illness score was associated with a 20% increase in the odds of being nonadherent to medications (OR 1.2, 95% CI 1.1–1.4; $P=0.003$).

Association between perceived barriers and medication nonadherence

As shown in Table 5, medication nonadherence was higher among patients who lacked transport to the health facility

Table 3 Association between sociodemographic and health-related factors and medication nonadherence

Characteristics	Nonadherent, n (%)	Adherent, n (%)	OR	95% CI	P-value
Sex					
Women	19 (55.9)	15 (44.1)	1		
Men	160 (76.4)	48 (23.6)	2.6*	1.2–5.6	0.01
Age-group (years)					
≥60	57 (66.3)	29 (33.7)	1		
18–59	122 (78.2)	34 (21.8)	1.8*	1.1–3.3	0.043
Marital status					
Married	156 (75)	52 (25)	1.4	0.7–3.3	0.365
Single	23 (67.7)	11 (32.3)	1		
Education level					
Tertiary	20 (83.3)	4 (16.7)	1		
Secondary or less	159 (72.9)	59 (27.1)	1.9	0.6–5.6	0.271
Monthly household-income level (RM)					
≥4,500	22 (88)	3 (12)	1		
<4,500	154 (73)	57 (27)	2.5	0.7–10	0.105
Employment status following MI					
Not working	64 (71.1)	26 (28.9)	1		
Working	115 (75.7)	37 (24.3)	1.1	0.6–2.1	0.63
Perceived current health status					
Good	128 (72.3)	49 (27.7)	1		
Poor	51 (78.5)	14 (21.5)	1.4	0.7–2.7	0.334
Diabetes					
No	96 (75.6)	31 (24.4)	1		
Yes	83 (72.2)	32 (27.8)	1.2	0.7–2.1	0.545
Hypertension					
No	57 (73.1)	21 (26.9)	1		
Yes	122 (74.4)	42 (25.6)	1.1	0.6–1.9	0.828
Hypercholesterolemia					
No	59 (65.6)	31 (34.4)	1		
Yes	120 (79)	32 (21)	2*	1.1–3.5	0.022
Time from MI event (months), mean	23.1	18.9	1.1*	0.9–1.2	0.041
Residence–hospital distance (km), mean	29.3	19.4	1.1*	0.9–1.2	0.045

Notes: *Statistically significant. Time from MI event and residence–hospital distance computed as continuous variables.

Abbreviation: MI, myocardial infarction.

(OR 5.9, 95% CI 1.4–25.5; $P=0.008$), those who preferred traditional medicines (OR 12, 95% CI 1.6–89.9; $P=0.002$), those lacking information about illness (OR 5.7, 95% CI 2–16.6; $P<0.001$), those fearing side effects (OR 9.4, 95% CI 3.9–22.9; $P<0.001$), and those with complex medication regimens (OR 4.9, 95% CI 2–12; $P<0.001$). These associations were statistically significant.

Factors associated with medication nonadherence using multiple logistic regression analyses

All statistically significant factors associated with medication nonadherence in the univariate analyses were included in the multivariate analyses. The multivariable model retained five statistically significant factors associated with medication

Table 4 Association between psychological attributes and medication nonadherence

Characteristics	Nonadherent, mean	Adherent, mean	OR	95% CI	P-value
Perceived life chaos	15.6	13.3	1.1*	0.9–1.2	0.003
Perceived denial of MI					
Denial of illness	4.8	3.7	1.2*	1.1–1.4	0.003
Denial of impact	10.8	10.3	1.1	0.8–1.3	0.37
Suppression	6.8	7.3	0.9	0.8–1.1	0.178
Perceived cardiac denial sum score	22.4	21.3	1.1	0.9–1.1	0.195

Notes: *Statistically significant. Psychological attributes computed as continuous variables.

Abbreviation: MI, myocardial infarction.

Table 5 Association between perceived barriers and medication nonadherence

Characteristics	Nonadherent, n (%)	Adherent, n (%)	OR	95% CI	P-value
Lack of transportation					
No	150 (71.1)	61 (28.9)	1		
Yes	29 (93.5)	2 (6.5)	5.9*	1.4–25.5	0.008
Prefer taking traditional medicine					
No	150 (70.8)	62 (29.3)	1		
Yes	29 (96.7)	1 (3.3)	12*	1.6–89.9	0.002
Lack of information about illness					
No	129 (68.6)	59 (31.4)	1		
Yes	50 (92.6)	4 (7.4)	5.7*	2–16.6	<0.001
Fear of side effects					
No	90 (61.2)	57 (38.8)	1		
Yes	89 (93.7)	6 (6.3)	9.4*	3.9–22.9	<0.001
Complex regimen					
No	118 (67.4)	57 (32.6)	1		
Yes	61 (91)	6 (9)	4.9*	2–12	<0.001

Note: *Statistically significant.

nonadherence: denial of illness (AOR 1.2, 95% CI 0.9–1.8, $P=0.032$), preference for traditional medicine (AOR 8.7, 95% CI 1.1–31.7; $P=0.044$), lack of information about the illness (AOR 3.3, 95% CI 1.1–10.6; $P=0.045$), fear of side effects (AOR 6.4, 95% CI 2.5–16.6; $P<0.001$), and complex regimen (AOR 5.2, 95% CI 1.9–14.2; $P=0.001$) (Table 6). The adjusted R^2 (Nagelkerke) showed that 39% of nonadherence was explained by this logistic model. The χ^2 goodness of fit was not significant ($P=0.862$), showing that the model had an adequate fit.

Table 6 Factors associated with medication nonadherence using multiple logistic regression analysis

Predictors	AOR	SE	Wald	95% CI	P-value
Hypercholesterolemia					
No	1	1	1	1	1
Yes	1.9	0.4	3.7	0.9–4	0.054
Denial of illness	1.2*	0.1	1.6	0.9–1.8	0.032
Prefer taking traditional medicine					
No	1	1	1	1	1
Yes	8.7*	0.9	4.1	1.1–31.7	0.044
Lack of information about illness					
No	1	1	1	1	1
Yes	3.3*	0.6	4	1.1–10.6	0.045
Fear of side effects					
No	1	1	1	1	1
Yes	6.4*	0.5	15.1	2.5–16.6	<0.001
Complex regimen					
No	1	1	1	1	1
Yes	5.2*	0.5	10.5	1.9–14.2	0.001

Notes: *Statistically significant. All significant variables in bivariate analysis. Denial of illness computed as continuous variable.

Discussion

This study aimed to determine the prevalence and factors associated with medication nonadherence among post-MI survivors in Malaysia. The prevalence of medication nonadherence was 74%. The estimated rate of medication nonadherence in this study was slightly lower than that found in South Korea (79%),⁴⁶ but relatively higher than that found in the UK (49.6%),⁴⁷ US (43%),¹⁵ Portugal (50.4%),⁴⁸ and Italy (37%).⁴⁹ The remarkably greater magnitude of medication nonadherence could be attributed to variations in sample size and study methodologies executed in previous studies or differences in local clinical practice guidelines adopted across different health-care settings in other countries. Akeroyd et al⁴ stated that the striking differences in medication-nonadherence rates between European and Asian countries could be attributed to differences in the methodologies used, acknowledging economic feasibility, resource-limited countries, and developing nations in Asia primarily use self-report measures to assess medication nonadherence compared to the “gold standard” measurements, such as pharmacy-refill data, used in developed countries.

Contrary to previous studies that found women to be nonadherent,^{9,10,50} this study found that medication nonadherence was more prevalent in men. This finding should be interpreted with caution, as the statistically significant association between sex and medication nonadherence could be attributed to the relatively high number of men recruited in this sample. This situation is unavoidable, as the incidence of MI among the Malaysian population is more prevalent in men than in women.^{51,52} Another plausible explanation of medication nonadherence among men is the apprehension of the medication side effects (erectile dysfunction with β -blockers),¹⁸ as evidenced in rigorous clinical trials.^{53,54}

Previous studies have shown mixed variations on the association between age and medication nonadherence: some argued that medication nonadherence was significantly higher in older groups as a consequence of impaired cognition, inadequate health literacy, and decline in physical or physiological functions,^{5,55} while others found significantly higher medication-nonadherence rates in younger groups that could be attributed to greater employment or social engagement.^{18,56} The statistically significant higher rates of medication nonadherence among younger groups in this study may agree with the latter notion. The authors found that medication nonadherence was higher among patients who traveled a longer distance to the health-care facility, and this association was statistically significant. Potential inhibitors may include difficult topography, lack of transport, or greater cost for travel.

Previous studies have deduced a significant association between medication nonadherence and time from MI event.^{5,57} This study found that patients with a longer time from the MI event were more likely to be nonadherent; however, the statistically significant association at the univariate level was eliminated in the final regression model. It is well known that post-MI patients are required to adhere to long-term cardioprotective drugs as a secondary prevention. This accelerates cost and possible side effects from prescribed medications, requiring adjustments of treatment regimen by cardiologists during follow-ups. This demotivates patients' belief in the benefits of newer drugs with an increased pill burden, predisposing them to a higher nonadherence rate.⁵⁷

This study found that the association between medication nonadherence with high-risk comorbidities (tendency to have high chances of post-MI fatality),^{28,58} like diabetes and hypertension, was not statistically significant. These findings were consistent with recent Italian⁹ and American⁵⁷ studies, but inconsistent with South Asian⁵⁶ and Malaysian⁵ studies. On the other hand, this study found a positive association between medication nonadherence and lower-risk comorbidity (tendency to have low chances of post-MI fatality),^{28,58} such as hypercholesterolemia. This finding is consistent with the South Asian⁵⁹ and Malaysian⁵ studies, but inconsistent with the Italian study.⁹ This paradoxical finding could be attributed to the "sick-stopper bias" (sicker patients are more likely to disengage themselves from the agreed treatment plan), and "healthy-user bias", which explains the better outcomes of less nonadherent patients.⁵⁶

Consistent with recent efforts by Zullig et al¹⁵ and Crowley et al,¹⁸ this study found a positive association between perceived life chaos and medication nonadherence. Populations being mobilized within the nation's fastest developmental phase and rapid urbanization are exposed to greater environmental noise, pollution, road traffic, employment competitiveness, rare neighborhood integration, and overcrowding.⁶⁰ Such situations impact one's health due to a chaotic lifestyle, apart from elevated frustrations of financial instability, loss of job, inappropriate housing, or inability to maintain clinic appointments as a sequel of MI,^{60,61} all of which form a risk for medication nonadherence.¹⁵

In contrast with previous studies, correlations between demographics and socioeconomic factors with medication nonadherence were eliminated in the final multivariable model. Perceived barriers were concurrent with the WHO domains-of-nonadherence framework.⁸ Patient-related factors (preference for traditional medicine), provider- and health system-related factors (lack of information about illness), and

therapeutic factors (fear of side effects, complex regimen) showed positive associations with medication nonadherence and were statistically significant. This significance could be attributed to multiethnic Malaysians' predilection for holistic health beliefs and complementary medicine use,¹⁴ in addition to physician adjustments to prescribed doses with newer synergistic therapies (in which patients may undermine the therapeutic efficacy or have greater concerns), can predispose patients toward medication-nonadherent behaviour.¹³

Denial of illness showed a positive association with medication nonadherence in the multivariate model. Lazarus⁶² initially proposed an intriguing hypothesis. He viewed denial as constructive at an early phase of the disease to overcome the emotional shock of the diagnosis, but found it destructive at a later course of disease progression, when active coping was needed. Fowers⁶³ supported this notion. He argued that at an early stage of an illness, denial was perceived as a coping mechanism to allay anxiety in cardiac patients, but over time these mechanisms collapse, implicating poor knowledge of cardiac disease progression and outcomes, delay in seeking treatment, and not being adherent to prescribed medications.⁶³

Study limitations

Limitations of this study should be acknowledged. The cross-sectional nature of this study could not ascertain temporal relationships. Although the adherence measure was validated, it may have been susceptible to social desirability bias as a self-report measure in this study, predisposing to overestimates of prevalence rates.

The relatively small sample from a single study site and the demographics of the study population (a majority men of younger groups) may limit the generalizability of the study findings, and thus extrapolation of the study findings is guarded. As noted in the results, the size of the study sample is reflected in its CI. The accuracy of the ORs, although significant, may not be wholly accurate. The CI reflects that the sample size was not adequate confidently to determine associations. Similarly, the findings that denial as a potentially new psychological factor was associated with medication nonadherence could be debated. The small sample could have been a reason for the statistically insignificant association between total denial score or other subdomain scores, like denial of impact and suppression with medication nonadherence. However, it should be noted that the sample-size calculation for this study was not done to predict this observation alone, but to involve other factors as well, including chaos, barriers to nonadherence, health

attributes, and sociodemographics. Therefore, there is a high tendency for the total denial score and other subdomain scores not to predict the main outcome measure. It should be noted that medication nonadherence is a vast subject with many dynamic variables, and it is not possible to explore all factors in one study. However, this cohort offered advantages that helped to offset concerns relating to the sample size, allowing the authors to address an existing evidence gap by exploring new variables as potential modifying targets in the psychological domain.

Conclusion

The remarkably high prevalence rate of medication nonadherence in this study showed a statistical significant association with patient-, provider-, and therapy-related barriers in line with the WHO framework.⁸ A new psychological factor, denial of illness, also showed statistical significance.

Recommendations

While the results suggest that emerging psychological attributes and patient- and therapy-related barriers influence medication-nonadherence rates, health-care professionals should be more vigilant in screening patients with a higher risk of poor adherence, including those patients prescribed complex regimens that require a change in lifestyle behaviors. Stratifying patients based on their adherence level would enable early, targeted interventions. In addition, it would be interesting to know whether high multimorbidity burden negatively affects post-MI medication adherence. Further exploration in future research is needed to assess such relationships across subgroups of common and different pathogenic pathways of diseases in addition to MI to determine the best possible outcomes for better policy and practice implications.

For patients living far from a health-care facility or those lacking transport, the revolution of big health data for virtual interconnectedness through mobile health could prompt health-care professionals to interact with patients regularly through WhatsApp, WeChat, Line, or Tango by sending friendly reminders for taking medication and exploring possible difficulties throughout the course of the treatment.⁶⁴ Community health nurses, pharmacists, doctors, and medical assistants could reach patients in rural areas far from current health-care facilities to provide follow-up care and prescribed medications through routine mobile health clinics.

Psychological factors like chaos and denial, which were tested for the first time in the Asian population, had significant or near-significant associations with medication

nonadherence; however, some of these factors lost significance in the multivariate analyses. While the present study hypothesized these modifiable factors to be significantly associated with medication nonadherence, it was not powered to reject definitively the null hypothesis to claim these attributes as predictors of nonadherence in post-MI patients. Future research should explore these attributes using robust methodological techniques, such as prospective cohort designs, to determine temporality between these factors.

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Author contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work. This study was part of a research-dissertation project performed by Dr Kurubaran Ganasegeran as fulfillment of his postgraduate Master's in Health Research degree under the supervision of Professor Dr Abdul Rashid at Penang Medical College.

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