**INTRODUCTION**

Dyslipidaemia, including elevated total cholesterol, is a lipoprotein metabolism disorder that results from overproduction or deficiency of lipoproteins. It is a feature of metabolic syndrome, in which a combination of medical disorders indicate a patient has greater risk of developing atherosclerosis. Cardiovascular disorders are now known as the world’s leading cause of death and disability; in 2015, it is estimated that more than 17 million deaths were attributed to cardiovascular disease, amounting to 31% of all deaths worldwide. The use of statin in Palestine is very common. In a retrospective study on 386 hospitalised patients, 113 (29.3%) had a documented previous statin use.

**Abstract**

**Aims:** Strong evidence indicates that drugs reduce blood lipids and improve cardiovascular end-points, leading to their wide usage. However, the success of these drugs can be affected by poor patient’s adherence to prescribed medication. This study aimed to evaluate medication adherence in patients with dyslipidaemia in association with patient beliefs about medicines.

**Methods:** The study was conducted from January 2019 to July 2019 at the middle governmental primary healthcare clinics in Ramallah and Bethlehem cities, and used a cross-sectional design. Adherence was determined using the 4-item Morisky medication adherence scale, while beliefs were determined using the Beliefs about Medicines Questionnaire.

**Results:** Of 220 patients, 185 agreed to participate in the study, resulting in a response rate of 84.1%. Of the participants, 106 (57.3%) were men, and almost half (88, 46.5%) were ≥56 years. Medication non-adherence was high (47.6%), but a majority (65.5%) reported believing their treatment to be necessary for their continued good health. Accordingly, the mean necessity score (17.3, SD 3.7) significantly outweighed \( P < .001 \) the mean concerns score (14.0, SD 3.5). Multivariate regression demonstrated four variables to be significantly correlated with non-adherence: illiterate (OR = 2.52; CI: 0.9-4.3; \( P = .03 \)), polypharmacy (OR = 3.18; CI: 1.9-5.7; \( P = .007 \)), having comorbidity (OR = 3.10; CI: 2.2-4.6; \( P = .005 \)) and having concerns about side effects (OR = 2.89; CI: 1.1-4.6, \( P = .04 \)).

**Conclusion:** Non-adherence among patients taking lipid-lowering agents was high despite most holding positive beliefs regarding medication necessity. This may be due to concern also being high. Physicians should identify and target high-risk patients and individualise their treatment plans in order to achieve adequate control of dyslipidaemia.
In treatment of chronic diseases, non-adherence to medication regimens is a key concern that can negatively impact treatment response, mortality and healthcare cost; consequently, this leads to elevated risk of hospitalisation, wasted resources, increased severity of disease and a need for more intense medicines. Medication adherence, the extent to which a patient take his medication as prescribed, is a multidimensional process to which many factors contribute. Factors related patients can include forgetfulness, interfering priorities, deliberately choosing to skip doses, being insufficiently informed and emotional considerations. Factors related to health provider can include the complexity of the medication regimen, insufficient education of patients on benefits and side effects, failure to consider the patient’s lifestyle or medication cost, and the lack of a good therapeutic relationship with the patient. Finally, factors related to healthcare system can include limited access of the patient to healthcare services, and the drugs and/or copayments having high costs.

The most powerful predictor of adherence is patient’s beliefs about their medicine, which multiple studies have shown to be significantly associated with adherence. As described by the Necessity-Concerns Framework, medication adherence is primarily affected by the patient’s expectation that their medication is required to maintain good health (necessity beliefs) and by worries about potential side effects (concerns beliefs).

To improve the overall outcome of dyslipidaemia treatment, it is important to evaluate medication adherence and patient beliefs about medication, and furthermore, to recognise factors affecting adherence. Nevertheless, in our setting, there is a lack of research on both adherence and patient beliefs. The goal of this study was to address this research deficit in patients with dyslipidaemia and to additionally evaluate the association of patient beliefs and other factors with medication adherence.

2 | AIM OF THE STUDY

This study aims to identify predictors of adherence to dyslipidaemia medication regimens, which will help to improve patient’s adherence and enhance awareness about the importance of lipid-lowering medications in those at high risk for coronary artery disease.

3 | METHODS

3.1 | Study design

This cross-sectional study was carried out between January and July 2019 at two middle governmental primary healthcare clinics in the cities of Ramallah and Bethlehem.

3.2 | Ethical approval

Before the initiation of this study, all aspects of the protocol were authorised by the Research Ethical Committee of Al-Quds University (ref no. 86/REC/2019) and by local health authorities at the study sites. The patients gave verbal consent forms before completing the questionnaires.

3.3 | Sample size and participants

Raosoft (http://www.raosoft.com/samplesize.html) was used to estimate the necessary sample size; 170 patients from both clinics participated in the study. Participants were recruited by means of convenience sampling and were selected from patients who were provided with medical care and anti-hyperlipidaemia medications at the selected healthcare centres with regular follow-up. A well-trained clinical pharmacist who works in a pharmacy clinic at the primary care conducted the interview.

Patients were included in the study if they: (a) were at least 18 years old; (b) were able to read or understand Arabic; (c) were willing to take part in the study; (d) were diagnosed with dyslipidaemia at least 1 year prior; (e) were currently being treated for dyslipidaemia and (f) these are lab results should be available in patients’ file and recordas mentioned in your previous question: lipoprotein (LDL) and total cholesterol.

3.4 | Measurement

The survey used contained four sections: socio-demographic factors obtained directly from patients; Morisky medication adherence scale (MMAS-4); the Beliefs about Medicines Questionnaire (BMQ); and clinical variables obtained from patient medical files.

In the MMAS-4, all questions had dichotomous responses (No = 0 and Yes = 1). Total scores were summed (range 0-4), with scores of 0-1 denoting high adherence and 2-4 denoting low adherence. The MMAS is perhaps the most widely accepted instrument for measuring self-reported medication adherence.
The BMQ was developed by Horne et al, and its Arabic version was validated for patients with chronic illness in 2012. This survey is composed of two 5-item scales; one assesses the perceived necessity of a medication for control of the patient's illness and the other concerns of adverse consequences from the medication. On both scales, each item is scored 5 to 1 (strongly agree to strongly disagree), with a higher score representing greater belief or concern; summing along a scale gives a total value of 5 to 25. Subtracting concern from necessity gives the necessity-concerns differential (NCD) score (−20 to 20), where a positive value indicates that the patient perceives medication benefits to outweigh risks and a negative value the inverse.

Patients were additionally categorised into four attitudinal profiles by dividing the scales at their midpoints (ie 15): 'indifferent' (both concern and necessity are low), 'sceptical' (concern high, necessity low), 'accepting' (necessity high, concern low) and 'ambivalent' (both concern and necessity are high).

3.5 | Statistical analysis

All data were coded and entered into SPSS, version 21 for all analyses. Continuous variables (eg, age, number of medications) were expressed as mean and standard deviation and categorical variables as frequencies (percentages). The Kolmogorov-Smirnov test was used to evaluate the normality of each variable. For categorical variables, significance was determined by either chi-squared or Fisher’s exact test; category means were tested for significant differences by Mann-Whitney test. A value of \( P < .05 \) was considered significant for analysis.

4 | RESULTS

4.1 | Patient characteristics

Of the 220 patients approached for this study, a total of 185 agreed to take part (response rate 84.1%). Of the 185 responders, 106 (57.3%) were men. Almost half of the participants (88, 46.5%) were ≥56 years of age; 79.7% widow; 42.7% were not educated; and 64.1% described themselves as religious. Two-thirds of participants (65.4%) reported school education, while only 22.2% were educated at the college or university level. Also, 119 (64.32%) had been prescribed with more than four drugs. Nearly all patients were taking statins (168, 90.80%) and had done so for an average duration of 8.6 ± 4.7 years; the mean total cholesterol of participants was 263.1 ± 52.1 mg/dL. Participant characteristics are detailed in Table 1.

4.2 | Non-adherence behaviours

In this study population, medication non-adherence as captured by 4-item MMAS was high (47.6%). Univariate analysis revealed that non-adherence was most likely among illiterate patients (\( P = .03 \)), those on more than four drugs (\( P < .001 \)) and those having comorbidities (\( P < .001 \)) (Table 1). Non-adherence was most commonly attributed to forgetfulness (35.2%), and second-most to insufficient care about taking medications (27.3%). Non-adherence was commonly unintentional (70.5%), and less often either intentional (26.1%) or mixed in intent (20.5%) (Table 2).

4.3 | Beliefs about medicines

Among participants in this study, a majority (65.5%) reported a strong belief in the necessity of their current treatment to maintain good health (ie not become ill). Lipid-lowering medications were additionally regarded as important for ensuring future health by most (52.7%) of the participants (Figure 1).

However, despite these beliefs, 60.1% of participants also reported concerns about their lipid-lowering medications having long-term or adverse effects. Overall, most participants (54%) were concerned about becoming dependent on lipid-lowering agents. There was much less concern about the medications disturbing their lives (Figure 2). Notably, the mean concern score of 13.21 (SD 3.2) was significantly below the mean necessity score of 17.92 (SD 3.2; \( P < .001 \)), for a mean necessity-concern differential of 4.7 (SD 1.4). However, individual necessity scores were lower (ie NCDs were negative) for 33 participants (17.8%), while equal scores were obtained for 8 participants (4.3%).

To group participants, their beliefs were categorised as high or low relative to the scale midpoints (specific-necessity and specific-concerns), defining four attitudinal categories: accepting—high necessity, low concern (93, 50.3%); ambivalent—high necessity, high concern (48, 25.9%); sceptical—high concern, low necessity (19, 10.3%) and indifferent—low concern, low necessity (25, 13.5%) (Figure 3).

Chi-squared analysis showed significant variation in non-adherence across attitudinal groups, \( \chi^2 (3, n = 185) = 13.47, P = .004 \). A majority (60.8%) of adherent patients were accepting, compared with 38.6% of the non-adherent group. In contrast, 78.9% of non-adherent patients were sceptical, compared with 21.1% of the adherent group.

4.4 | Association of beliefs with other factors

Analysis revealed that adherent patients more strongly believed they had personal need of lipid-lowering drugs. Meanwhile, non-adherent participants possessed stronger concerns about long-term use of medications and potential adverse events in the future (Table 3). The NCD score of non-adherent participants was lower than that of adherent participants (4.7 vs 1.7, \( P < .001 \)), revealing that for non-adherent participants belief in the need for lipid-lowering agents was similar to concern about long-term use of the medications.

Table 4 gives additional results correlating necessity scores with patient characteristics. The mean necessity score for men was
not significantly greater than that of women (17.7 vs 16.8, \( P = .14 \)).

However, a significant negative correlation was observed when considering total cholesterol (\( P = .03 \)) or Morisky score (\( P = .01 \)). No significant association was identified that connected any other demographic or clinical variables with necessity scores.

Unlike necessity scores, concern scores were found to have significant associations with demographic and clinical variables (Table 5). Namely, significant positive correlations were identified with the number of medications being taken (\( P = .01 \)) and Morisky score (\( P = .01 \)). No significant correlations were identified for other demographic or clinical variables.

Associations of independent variables with low adherence were predicted using a stepwise multivariate logistic regression model (Table 6). Four variables were identified as significant and associated with non-adherence: illiterate (OR = 2.52; CI: 0.9-4.3), polypharmacy (OR = 3.18; CI: 1.9-5.7), having a comorbidity (OR = 3.10;
For this analysis, patients were only considered adherent if scored as high adherence (score of 0-1); those who scored >1 were considered to have low adherence. More than 90% of participants were taking statins, and 47.6% self-reported low adherence. Our findings are inconsistent with previous studies, which determined that 30%-50% of patients stopped taking lipid-lowering medication and that adherence decreases over time. The most likely causes of low adherence in our sample were unintentional forgetfulness and carelessness in taking medications, which were reported by 35.2% and 27.3% of patients, respectively. However, nearly a fifth of patients (19.3%) reported intentional non-adherence in that they stopped taking their medications upon feeling better. The overall non-adherence rate (46.7%) in this study concurs with prior reports by Elsous et al (52.3%), Jackson et al (51.2%) and Bizu et al (51%). However, lower adherence rates have also been reported by Sweileh et al at 16.9% and 42.7%, respectively.

In this study population, non-adherence was primarily caused by unintentional behaviours, most commonly forgetfulness and carelessness about medication time. Reasonable explanations for these behaviours may be attributed to multiple factors, including work, travelling, economic status and lack of effectiveness or adverse effects of the medications. The main finding concerning beliefs about medicines was that the majority of patients having dyslipidaemia hold strong beliefs with regard to medication necessity (mean necessity score 17.3). However, a high proportion of participants also expressed concerns about long-term and potential adverse effects. A general practice survey in France, revealed that more than 10% of patients with dyslipidaemia receiving high-dose statins reported myopathy symptoms. Another study in the United States called (USAGE) reported myopathy side effects in 60% of current and 25% of former users, with side effects the primary reason for statin discontinuation (62%). The importance of patient perception of side effects in adherence has been demonstrated by several studies, and non-adherence may be particularly likely for patients on high doses of cholesterol-lowering drugs who experience adverse events.

In this study, no association was identified connecting necessity score with the demographic variables of age, duration of dyslipidaemia or the number of drugs being taken. However, necessity scores were negatively associated with mean Morisky medication adherence (low score meaning higher adherence) and with total blood cholesterol level. This finding is reasonable as better adherence with lipid-lowering agents will result in a decrease of total cholesterol in the blood. Meanwhile, significant and positive associations with concern scores were observed for Morisky score, high blood cholesterol level, and number of medications taken. Our findings are in accordance with prior reports in US specialist care and in the context of various long-term conditions.

### Table 3: Necessity and concern scores for adherent and non-adherent patients

<table>
<thead>
<tr>
<th>Score</th>
<th>Adherent Mean (SD)</th>
<th>Non-adherent Mean (SD)</th>
<th>t (df)</th>
<th>Mean difference</th>
<th>95% CI</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necessity score</td>
<td>17.92 (3.2)</td>
<td>16.63 (4.1)</td>
<td>2.4 (185)</td>
<td>1.29</td>
<td>0.23-2.3</td>
<td>.018</td>
</tr>
<tr>
<td>Concerns score</td>
<td>13.21 (3.2)</td>
<td>14.91 (3.7)</td>
<td>−3.3 (185)</td>
<td>−1.69</td>
<td>−2.70 to −0.68</td>
<td>.001</td>
</tr>
<tr>
<td>NCD</td>
<td>4.7 (1.4)</td>
<td>1.7 (0.16)</td>
<td>3.5 (185)</td>
<td>2.96</td>
<td>1.33-4.54</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; df, degrees of freedom; NCD, necessity-concerns differential; SD, standard deviation.

* t test.
Patient adherence was further evaluated in terms of attitude by combining necessity and concern ratings in a two-dimensional analysis. Half of the participants (50.3%) classified as accepting of their lipid-lowering agents (high necessity, low concern). Participants who were classified as sceptical (high concern, low necessity) were more likely to have low adherence.

Logistic regression revealed several factors predictive of non-adherence behaviours: illiteracy and low education (at most through primary school) were the most likely predictors (P = .03). Many previous studies have similarly reported higher rates of non-adherence among patients of lower education levels.29,30 Lower education is also associated with lower socio-economic status, poor access to the health system and less knowledge about their disorder.31 Thus, providing more accessible facilities and arranging educational and training programs can improve treatment adherence.32

Polypharmacy (having more than four drugs prescribed) was found to be highly predictive of non-adherence (P = .007). A review analysis by Zelko et al33 found that for polypharmacy patients, non-adherence rates ranged from 6% to 55%. Valladolid et al have found negative associations of medication adherence with more drugs being taken, a large cost burden.34 In the present study, co-morbidity was another highly significant predictor of non-adherence (P = .005). Our findings are consistent with the literature, which have reported association of comorbidities with depression, anxiety and stress, which then have negative effects on adherence.35

The last independent predictor of non-adherence identified in this analysis was concern about medications (P = .04), consistent with prior literature.36 Consideration of patient concerns may be essential in ensuring adherence and effective use of medication; patient concerns have been found to predict non-adherence in terms of both extent and direction (over- or underuse).37

When developing strategies to improve adherence, modifiable factors should be addressed, and the patients targeted should be those most likely to not adhere. However, the currently available literature on adherence is highly heterogeneous; efforts are first needed to improve the standardisation and therefore comparability of adherence studies.
Patient education and information have been shown to lead to enhanced knowledge and improved lipid-control behaviours. A systematic review of seven studies involving educational and knowledge interventions found that participants who received an intervention were more adherent than those who received only usual care (odds ratio 1.93, 95% confidence interval 1.29-2.88).

The results of this work indicate that patients with risk factors pay more attention. Accordingly, patient beliefs about the risks of high cholesterol and the severity of high cholesterol are significantly associated with medication compliance, and adherence then reinforces the beliefs. Other studies have reported that patient beliefs about the importance of cholesterol in heart disease incidence will increase patient motivation and increase adherence. Meanwhile, patients who lack understanding of the risks associated with high cholesterol may be less likely to believe the condition is serious and that aggressive treatment is necessary.

Pharmacists can enhance adherence among patients with dyslipidaemia. A number of interventions that involve pharmacists have been documented in the literature, including counselling visits at the pharmacy, making phone calls and leaving voice messages, telephone counselling coordinated by a computer-based tracking system, and preparing a ‘beep card’ to provide reminders when a dose is due.

5.1 Strength and limitations

This study was unique in classifying attitudes of patients having dyslipidaemia towards their medications as four attitudinal categories: accepting (high necessity/low concern), ambivalent (high concern/ high necessity), sceptical (high concern/low necessity) and indifferent (low concern/low necessity).

Surveys and self-reported methods have potential limitations, which are prone to recall biases and/or overestimation of adherence rate may have occurred. Due to the nature of the study as a questionnaire-based study, explaining the cause and effect of non-adherence is limited. Finally, the study covered only two medical centres, which may lack generalisability of our findings.

6 CONCLUSION

This study contributes to the increasing evidence suggesting that patient concerns and beliefs about medication are associated with adherence behaviour. In addition, direction of non-adherence was related to specific types of concern. Patient concerns, long-term effect and experiencing side effects appear more pivotal in determining non-adherence than both level of LDL and cholesterol.

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DISCLOSURES

None.

AUTHOR CONTRIBUTIONS

All authors contributed to study conduct and design. MK and JS oversaw study design, HA and DA acquired data. All authors interpreted data. HH and MK prepared and revised the manuscript. All authors read and approved the final manuscript.

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