

Research Article

The Effects of a Health Literacy Training Intervention on Self-Care Behaviors and Treatment Adherence in Patients with Ischemic Heart Diseases

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Abstract

Objectives: This study examined the effect of a health literacy training intervention on self-care behaviors and treatment adherence in patients with ischemic heart disease (IHD).

Methods: A quasi-experimental study was conducted in 2020, on 50 patients with IHD referred to a medical center in Kashan, Iran. The patients were assigned to a control group (n=25) and an intervention (n=25) group via a block randomization method. The intervention group received a health literacy training intervention, while the control group did not. The "Adherence to Treatment Questionnaire" and the "Self-Care Behavior Questionnaire" were used to gather the data at the start and the end of the study.

Results: The mean baseline self-care behaviors in the intervention and the control groups were 61.56 ± 10.99 and 56.25 ± 8.42 ($p=0.061$) out of 100, which then changed to 85.24 ± 4.06 and 53.01 ± 4.86 ($p<0.001$). Also, the mean baseline treatment adherence in the intervention and the control groups were 84.77 ± 29.19 and 84.40 ± 13.89 ($p=0.315$) out of 200, which then changed to 179.08 ± 8.59 and 95.76 ± 9.24 ($p<0.001$).

Conclusion: The health literacy training intervention could improve self-care behaviors and treatment adherence in patients with IHD. Nurses and the medical team are recommended to implement similar packages to improve the health literacy of patients with IHD.

Keywords: Health literacy, Patients education, Ischemic heart disease, Self-care behaviors, Treatment adherence

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Ischemic heart disease (IHD) is one of the leading causes of death worldwide. In 2017, IHD affected about 126 million people globally. At the same time, this disease has caused 1599 deaths and 2149 cases of disability per 100,000 people in Iran, respectively.^[1] Despite the global prevalence of IHD, between 30 and 60% of these patients do not have adequate self-care and do not adhere to their treatment recommendations.^[2, 3]

Treatment and prevention of IHD require lifestyle changes and adherence to health care recommendations, both of

which require a proper understanding and interpretation of health information.^[4] However, research has shown that about half of patients with cardiovascular disorders have do not have sufficient health information, 54% cannot find health information, and more than 44% do not fully understand the information they receive from the healthcare providers.^[5]

Patients' perceptions of health care recommendations are believed to be associated with their health literacy (HL) level.^[6] HL is defined as the extent to which an individual

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can obtain, process, understand and use the health information and services needed to make appropriate health-related decisions.^[7] HL does not simply mean knowing, but includes a set of skills, abilities, and capacities to obtain medical and health information, and apply them in health-related decisions.^[8] Patients' HL has been reported to affect their recovery and quality of life.^[9] However, low HL is a challenge in both developing and developed countries.^[10, 11] A systematic review has reported that HL is low in Southeast Asian countries.^[12] A study also reported that approximately 80 million adults in the United States have limited or low HL.^[13] A study in Iran has also reported that public HL is low.^[14] Low levels of HL can lead to unnecessary medical visits, increased problems with medication use, prolonged hospital stays, and increased patient and health system costs.^[15, 16] Therefore, promoting patients' HL is a top priority for health care providers and healthcare systems.^[17]

Self-care and adherence to health care recommendations are also crucial factors affecting disease prevention and management,^[3] quality of life,^[18] and the frequency of medical visits and hospital readmissions.^[19] Inadequate self-care is associated with poor health^[20] and frequent hospital readmissions.^[21] In contrast, decreasing potentially modifiable risk factors, and increasing appropriate self-care behaviors, can not only prevent the progression of IHD, but also promote collateral coronary artery perfusion, improve myocardial perfusion,^[3] reduce hospital readmissions, and increase the patients' one-year survival.^[22] However, an interventional study of patients with IHD showed that the patients' baseline scores of self-care ability were considerably low, showing that they did not adopt suitable self-care behaviors.^[23] Another study also reported that a majority of patients were non-adherent to dietary, exercise, and medication recommendations after the coronary artery bypass grafting surgery (CABG).^[24]

Patient education is a common intervention to promote self-care and treatment adherence.^[23, 25] Studies have shown that patient education can motivate patients to monitor symptoms, take medication, and adhere to medical advice.^[23, 26] Dessie et al. (2021) also examined the effects of patient education on self-care in patients with heart failure and reported the positive effects of the intervention.^[25] Similarly, Barkhordari-Sharifabad et al. (2021) conducted an educational program to improve the self-care of patients with heart failure, but instead of conventional lectures, they used a virtual system to send educational materials such as texts, photos, animations, and videos, to patients. They have reported that this innovative method was significantly effective in improving the patients' self-care behaviors.^[26] Nonetheless, Adib-Hajba-

ghery and Karimi (2018) have reported that virtual and mobile-based education for chronic conditions, might not be as effective as face-to-face educational methods.^[27] Some interventional studies also focused on patients with IHD and reported that educational interventions could improve self-care, quality of life,^[28] and treatment adherence,^[29] of these patients. Although these studies focused on patient education, they did not address the concept of HL.

Considering the importance of HL, and its difference from mere knowing or being skilled in specific areas,^[8] some descriptive and correlational studies assessed the HL of patients with IHD and its influencing factors.^[5, 7, 30, 31] However, limited studies have examined the effects of interventions on HL in patients with IHD, or the effects of HL interventions on self-care or treatment adherence in these patients. In one of the few studies conducted in Iran, Miri et al. have examined the HL of 75 patients with IHD who underwent CABG surgery and reported that most of the patients had inadequate HL. They also reported that patients with higher HL experienced shorter hospital stays and fewer postsurgical complications.^[7]

A number of studies have also reported that HL can predict patients' health behaviors, self-reported health,^[32] quality of life,^[30] medication adherence,^[31] and morbidity and mortality.^[33] However, some studies on patients with heart diseases have reported that although HL affects the patients' knowledge, it has little effects on their self-care behaviors and treatment outcomes.^[34, 35] In the only interventional study on HL of Iranian patients with IHD, Fallahi and Miri reported that e-learning improves the HL of these patients. However, this study was not blind, its sample size was small, the duration of intervention was short (two weeks), neither reported the patients' clinical outcomes nor the effects of the intervention on self-care behaviors and adherence to the healthcare recommendations.^[36] Given the high prevalence of IHD, and the importance of self-care behaviors and adherence to healthcare recommendations, and because few interventional studies have been conducted in Iran to examine the impact of HL on self-care behaviors and treatment adherence in patients with IHD, and also due to the controversies about the effectiveness of absolutely virtual training methods, this study was conducted with the aim of examining the effects of a health literacy training intervention—which comprised of a combination of virtual and face-to-face educations—on self-care behaviors and treatment adherence in patients with IHD. The primary and the secondary outcomes of the study were the patients' mean scores of self-care behaviors and treatment adherence.

Methods

A quasi-experimental study was conducted from February to September 2020, on 50 patients with IHD referred to Shahid Beheshti Hospital in Kashan, Iran. This is the largest government hospital in Kashan and is affiliated with the Kashan University of Medical Sciences. It has general and specialty wards and is the main referral center for cardiac patients in Kashan. Besides several general and specialty units, the hospital has two coronary care units (CCU), two post CCU wards, two medical cardiac wards, and an outpatient clinic that covers patients with cardiac conditions.

The sample size was calculated using a pilot study on eight patients with IHD. The patients' mean score of self-care behaviors changed from 57.32 ± 6.81 to 63.65 ± 8.53 three weeks after the training sessions. Then, using the formula for the comparison of two means, with 95% confidence level, 80% test power, μ_1 of 57.32, μ_2 of 63.65, δ_1 of 6.81, and δ_2 of 8.63, the sample size was calculated to be 24 for each group. However, we recruited 25 patients per group.

Inclusion criteria were: a medical diagnosis of IHD, age between 18 and 65 years, lack of known cognitive disorders, inclination to participate in the study, ability to speak and read and write in Persian, stability of clinical condition and lack of pain during the study, referring to the Shahid-Beheshti Hospital for follow-up or for treating the recurrence of symptoms, having a Smartphone, and being able to exchange experiences in the intended social network. Exclusion criteria included a decision to withdraw from the study or the intended social network, participation in similar training programs during the study, absenteeism in one of the training sessions, death of the patient, and occurrence of any critical conditions needing hospitalization or prevent from the participation in the study.

Sampling was performed consecutively, and the patients were randomly assigned to the intervention and control groups using a block randomization method. Before data collection, the study supervisor prepared a permuted block randomization schedule using an online number generator (i.e., <https://www.sealedenvelope.com/simple-randomiser/v1/lists/>) and the supposed participants were randomly allocated into 9 blocks of 6 to be assigned to a control or an intervention group, 25 in each group (Fig. 1).

The participants who met the inclusion criteria were identified and invited to the study by daily reviewing of the files of patients admitted to cardiac care units, medical wards, and the outpatient department of Shahid-Beheshti Hospital, Kashan, Iran.

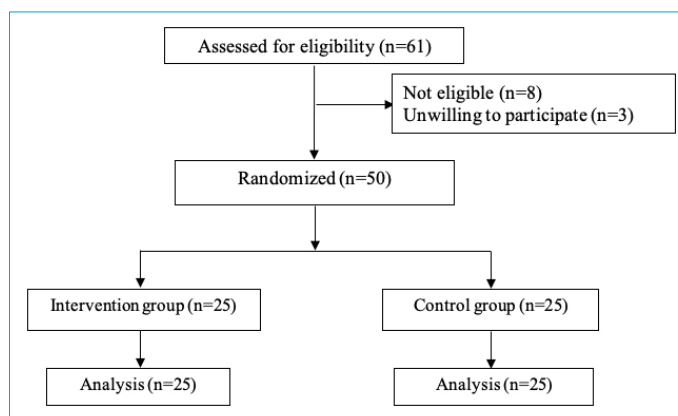


Figure 1. The study flow diagram.

Data Collection Instruments

A three-part instrument was used to gather the data including a personal information form, the Modanloo's Adherence to Treatment Questionnaire (MATQ),^[37] and the Self-Care Behavior Questionnaire (SCBQ).^[38] The personal information form included items on the patients' age, sex, marital status, job, height, weight, Body Mass Index, education level, adequacy of income, place of residence, having other comorbidities, source of information about illness and care, frequency of hospitalization for heart disease in the last 12 months, and the number of medical visits for heart disease in the last 12 months.

The MATQ consists of 40 items in seven subscales namely making the effort for treatment (9 items; e.g. "I insist on the treatment even when it disrupts my social activities"), willingness to participate in the treatment (7 items; e.g. "I eagerly follow the recommendations of the treatment team"), ability to adapt (7 items; e.g. "I regulate my daily life according to my treatment plan"), integration of treatment into life (5 items; e.g. "The simpler the treatment recommendations, the easier to integrate them with my life schedules"), sticking to the treatment (4 items; e.g. "I do not give up my treatment under any circumstances even at parties, work, travel, holidays and weekends"), commitment to treatment (5 items; e.g. "I do not stop my treatment during the recovery period or as the symptoms of the disease decrease"), and careful implementation of treatment (3 items; e.g. "The contradictory recommendations of the treatment team do not stop me from continuing the treatment"). All items are answered on a five-point Likert scale from "5: absolutely important" to "1: not important at all". The overall score can range between 40 and 200. The higher score shows the better adherence. According to the instructions of the questionnaire designer, the scores 40-80, 81-120, 121-160, and 161-200 are considered as weak, moderate, good, and very good adherence, respectively. They also suggested that all the scores can be converted to a 0 to 100 scale; then, the

lowest and highest possible scores would be set at 0 to 100 points and the scores 0-25, 26-49, 50-74, and 75-100 would be considered as weak, moderate, good, and very good adherence, respectively. Seyed Fatemi et al. evaluated the validity and reliability of the MATQ and its Cronbach's alpha was reported 0.921.^[37]

The SCBQ was developed specifically to measure the extent to which people with cardiac diseases perform five types of prescribed self-care behaviors including adherence to the diet (e.g. "I follow the prescribed diet even at work"), limiting smoking (e.g. "I observe smoking restrictions at home as recommended by my doctor), performing activities (e.g. "I follow the prescribed activities when I participate in social activities"), taking medications (e.g. "I take the prescribed medicine when I exercise or have fun"), and changing responses to stressful situations (e.g. "I modify my responses to situations that upset me at home).^[38] It contains 20 self-report items that are responded on a five-point Likert scale ranging from 1= unlikely to 5 =likely.

Each subscale includes four items with a maximum score of 20. To obtain the total score, the sum of all five subscales is calculated to produce a score between 20 and 100. A higher score indicates better self-care behavior. The validity and reliability of the Persian translation of this scale were assessed by Niknam et al. and the Cronbach's alpha for different subscales ranged from 0.80 to 0.98.^[39] All the patients completed the personal information form, the MATQ, and the SCBQ at the beginning of the study.

Intervention

The HL training intervention included three components: 1) two individual face-to-face training sessions; 2) an educational booklet; and 3) the creation of a group in one of the social networks for continuing education and exchanging experiences and information.

Because the study coincided with the coronavirus-2019 (COVID-19) pandemic, individual training sessions with observing social distancing, masks, suitable ventilation of the training room, and other preventive precautions were designed for each patient. Therefore, for each patient, two face-to-face training sessions were held for 1-2 hours with an interval of two days. Patients were asked to bring their prescribed medications with them. After greeting, in the first training session, the patients were asked to briefly explain their typical day with a special focus on their activities, medication use, regimen, and cardiac problems experienced. Then, using a computer and PowerPoint, the first researcher provided them with information about the nature of the disease, its complications, risk factors, and principles of medication therapy. The second session usually started with discuss-

ing about accepting and following the medication regimen, and continued with materials on a proper nutritional pattern, weight loss (if needed), methods of problem-solving and stress reduction, regular moderate physical activity, and smoking cessation. Totally, 50 individual training sessions were held during the study. All the training sessions were held in a private room in the outpatient clinic of the aforementioned hospital. At the end of the second training session, a booklet containing the necessary educational material about IHD and how to manage treatments was provided to every patient. The educational booklet included information about the disease, dietary and medication regimen and related care, appropriate physical activities and exercises, lifestyle modification, addresses of some websites containing valid information on health and tips on how to interpret and process health information needed for cardiovascular patients, and the importance of taking responsibility for self-care and appropriate health behaviors.

In the intervention group, each patient was also invited to join an educational group created in one of the social networks, through it — for 5 weeks— they regularly received training messages and educational media about diet and physical activity in IHD, stress management, how to take the prescribed medications, and follow the medication-related care. It was also possible for all patients to exchange their information and experiences through the social network.

Patients in the control group did not receive the intervention. At the end of the eighth week, patients in the two groups were contacted, and individual appointments were made with them to complete the MATQ and SCBQ again. All of the training sessions and the communications in the social network as well as data collection were managed by the first researcher (i.e. ZH) who is an experienced nurse.

Ethical Considerations

The study protocol was approved by the Research Council and the Ethics Committee of Kashan University of Medical Sciences, Kashan, Iran (approval number: IR.KAUMS.NUHEPM.REC.1398.040). At the beginning of the study, the patients and one of their family members were given explanations about the purpose and research method. They were also informed about their right to either participate in or withdraw from the study at any time. All patients also signed a written informed consent form at the onset of the study and were assured of the confidentiality of their personal information.

Data Analysis

After coding and entering the data into the SPSS 16 software (SPSS Inc., Chicago, USA), the characteristics of the

patients were described using descriptive statistics, including frequency, mean, and standard deviation. The Chi-square or the Fisher's exact tests were used to compare the categorical variables between the two groups. The normal distribution of quantitative variables was examined using the Kolmogorov-Smirnov test. The paired and the independent samples t-tests were used, respectively, for within and between-group comparisons of means of variables with normal distribution. The Wilcoxon or the Mann-Whitney U tests were respectively used if the variables did not follow the normal distribution. The statistical significance was set at <0.05 .

Results

The mean ages of the intervention and control groups were 64.40 ± 11.22 and 88.67 ± 10.79 , respectively. Also, patients in the intervention and control groups had an average of 11.80 ± 9.41 and 11.92 ± 7.88 medical visits for their heart disease during the last 12 months. A majority of the patients in the intervention group (80%) and the control group (64%) were males. Most of the participants in both groups were married (96%), were educated lower high school diploma (88%), lived in the city (60%), and had additional comorbidities (76%). The two groups were homogenous in all personal characteristics ($p > 0.05$, Table 1).

Table 1. Demographic characteristics of the intervention and the control groups

Variables	Group		p
	Intervention, Mean \pm SD or n (%)	Control, Mean \pm SD or n (%)	
Age	64.40 \pm 11.22	67.88 \pm 10.79	0.269 ^a
Height	163.84 \pm 7.94	161.40 \pm 21.69	0.600 ^a
Weight	70.28 \pm 9.75	73.20 \pm 11.06	0.327 ^a
Body Mass Index	26.49 \pm 3.01	25.66 \pm 3.48	0.375 ^a
Frequency of hospitalization for heart disease in last 12 months	1.44 \pm 1.19	1.44 \pm 0.91	0.999 ^a
Number of medical visits for heart disease in last 12 months	11.80 \pm 9.41	11.92 \pm 7.88	0.961 ^a
Sex			0.208 ^b
Female	5 (20)	9 (36)	
Male	20 (80)	16 (64)	
Marital status			0.999 ^c
Single	1 (4)	1 (4)	
Married	24 (96)	24 (96)	
Job			0.856 ^c
Self-employed	3 (12)	3 (12)	
Unemployed	9 (36)	7 (28)	
Retired	13 (52)	15 (60)	
Education level			0.999 ^c
Lower diploma	22 (88)	22 (88)	
High school diploma	3 (12)	3 (12)	
Adequacy of income			0.113 ^c
Sufficient	6 (96)	4 (16)	
Fairly sufficient	14 (56)	9 (48)	
Insufficient	12 (48)	5 (20)	
Place of residence			0.564 ^b
City	14 (56)	16 (64)	
Suburbs	11 (44)	9 (36)	
Having comorbidities			0.321 ^b
Yes	17 (68)	21 (84)	
No	8 (32)	4 (16)	
Source of information about illness and care			0.121 ^c
Healthcare team	12 (48)	16 (64)	
Media and friends	5 (8)	7 (28)	
None	8 (44)	2 (8)	

^at-test, ^b chi-square test, ^c Fisher's exact test.

As Table 2 shows, after the intervention, the mean scores of self-care behaviors and treatment adherence increased significantly in the intervention group, but the changes in the control group were not statistically significant.

Table 3 also shows that at the beginning of the study, the mean scores of the five subscales of self-care behaviors did not differ significantly between the two groups ($p>0.05$). However, at the end of the intervention, the mean scores of

the five subscales of self-care behaviors were significantly higher in the intervention group compared to the control group ($p<0.05$).

Furthermore, at the beginning of the study, the mean scores of treatment adherence subscales did not significantly differ between the two groups ($p>0.05$). However, at the end of the intervention, the mean scores of the subscales were significantly higher in the intervention group compared to the control group ($p<0.05$, Table 4).

Table 2. Comparison of the mean self-care behavior and adherence to treatment between the intervention and the control groups

Group	Time		p
	Before the intervention ^a	After the intervention ^a	
Self-care behavior			
Control	56.25±8.42	53.01±4.86	0.102 ^d
Intervention	61.56±10.99	85.24±4.06	<0.001 ^d
p	0.061 ^b	<0.001 ^b	-
Adherence to treatment			
Control	84.40±13.89	95.76±9.24	<0.001 ^e
Intervention	84.77±29.19	179.08±8.59	<0.001 ^e
p	0.315 ^c	<0.001 ^b	

^aData presented as mean ±SD, ^bt-test, ^cMann-Whitney U test, ^dPaired t-test, ^eWilcoxon test.

Discussion

The present study showed that receiving a HL training package could significantly increase the overall mean scores of self-care behaviors and four out of its five dimensions. In other words, it has significantly improved the patients' self-care behaviors in the dimensions of diet, smoking restriction, taking medications, stress avoidance, and maintaining peace of mind, although could not considerably affect on physical activity. It seems that low HL is an obstacle to the understanding of the importance and severity of the IHD and diminishes self-care. However, an increase in the HL of patients with IHD can improve their self-care behaviors. However, the trivial change in patients' physical activity can be attributed to their advanced age, and that a significant increase in physical activity may have

Table 3. Comparison of the mean self-care behavior between the intervention and the control groups

Variables	Before the intervention ^a			After the intervention ^a		
	Control group	Intervention group	p ^b	Control group	Intervention group	p ^b
Adherence to the diet	10.04±1.39	9.92±2.58	0.839	11.08±1.75	18.40±1.32	<0.001
Smoking restriction	12.56±3.11	14.64±4.71	0.071	10.48±1.35	19.04±1.3	<0.001
Physical activities	10.19±1.32	11.28±2.49	0.059	9.92±1.32	11.84±2.35	0.020
Taking medications	12.29±2.36	13.28±1.02	0.060	8.01±1.75	23.76±0.83	<0.001
Changing responses to stressful situations	11.92±2.43	12.44±3.74	0.563	13.52±2.02	22.76±1.53	<0.001

^aData presented as mean±SD, ^bMann-Whitney U test.

Table 4. Comparison of the mean treatment adherence between the intervention and the control groups

Variables	Before the intervention ^a			After the intervention ^a		
	Control group	Intervention group	p ^b	Control group	Intervention group	p ^b
Effort for treatment	18.60±3.73	16.24±7.17	0.151	21.56±2.43	40.72±1.90	<0.001
Willingness to participate in the treatment	14.84±3.31	14.12±6.22	0.612	16.72±3.08	31.20±1.80	<0.001
Ability to adapt	15.24±2.48	14.60±5.83	0.616	16.84±2.30	31.76±1.78	<0.001
Integration of treatment into life	10.64±2.51	9.48±4.15	0.238	11.92±1.41	22.80±1.52	<0.001
Sticking to the treatment	8.72±1.98	7.68±2.83	0.140	10.08±0.08	17.60±1.32	<0.001
Commitment to treatment	10.16±2.30	9.60±3.34	0.494	11.92±2.27	21.76±2.02	<0.001
Careful implementation of treatment	6.20±1.29	6.12±2.60	0.891	6.78±1.17	13.24±1.20	<0.001

^aData presented as mean±SD, ^bMann-Whitney U test.

been more difficult for them than changing other self-care behaviors. SheikhSharafi and Seyedamini,^[8] as well as Aaby et al.,^[32] have reported a significant relationship between HL and self-care behaviors. Matsuoka et al.^[40] also reported that patients with low HL have low self-care behaviors compared to those with high HL.

The current study also illustrated that the HL training package could significantly improve the overall mean score of treatment adherence and all its subscales. In other words, the HL training package has doubled patients' mean scores in all subscales of treatment adherence. It increased their effort for and willingness to participate in the treatment; increased their ability to adapt and integrate the treatment in their life, increased their commitment to treatment, stuck them to the treatment, and caused them carefully implement the treatment. It appears that the low HL of patients with IHD is a barrier to understanding and following the healthcare and treatment recommendation provided by the healthcare providers. On the other hand, increasing HL in patients with IHD improves their adherence to treatment and health care recommendations. Zullig et al. also conducted a six-month pilot HL intervention focusing on medication literacy in 23 outpatients with cardiovascular risk factors and reported that the HL intervention could improve the patients' self-reported medication adherence at third month but no significant changes were observed in clinical outcomes such as blood pressure, pulse, weight, and lipid profile at the end of the study.^[41] Although the patients' characteristics in Zullig et al.'s study are comparable to the characteristics of our patients, however, because of the small sample size and lacking a control group, their results should be interpreted with caution. However, together with other studies,^[41-43] and in line with our findings, it can be concluded that HL interventions can improve treatment adherence in patients with IHD and those with cardiovascular risk factors. Oscalices et al. in a cross-sectional study also studied HL and treatment adherence of patients with heart failure and reported that the low level of HL was directly related to lower treatment adherence, higher rates of hospital readmissions, and death.^[43] A meta-analysis on correlational and intervention studies examining the relationship between HL and adherence to medication regimens in patients with cardiovascular diseases also concluded that higher levels of HL were positively associated with higher adherence to diet and medication-related recommendations.^[42] Nonetheless, in a study of patients with rheumatoid arthritis, Quinlan et al. (2013) have reported that HL is associated with medication knowledge but not medication adherence. Instead, patients' race, access to neighborhood resources, and trust in health care providers were predictors of adherence.^[44] In the present study, we did not assess

the effects of factors such as race, neighborhood resources, and trust to healthcare providers, and the sample size was not enough to reliably conduct a subgroup analysis, however, it seems that people with inadequate HL are less likely to understand the written and verbal information provided by health professionals and to follow their instructions. It has been reported that people with low HL have poorer health which consequently increases their medical costs.^[45] In our study, this fact is reflected in the finding that most of the participants suffered from additional comorbidities, that may negatively affect their overall health and medical costs. Therefore, according to the results of this study and other studies in this field, HL is an important factor in patients' self-care behavior and treatment adherence. Increasing the HL of patients with IHD will improve their understanding of health information, and promotes their self-care behaviors and treatment adherence. This in turn will improve patients' health and reduce treatment costs.

This study had limitations that should be considered. The sample size of this study was small. Also, due to the nature of the intervention, it was not possible to blind the intervention group. Also, the first author who implemented the study intervention was also the one who gathered the study data. Nevertheless, designing larger, multicenter, and blinded studies is recommended.

Conclusion

The implementation of the HL package could improve self-care behaviors and treatment adherence in patients with IHD. Therefore, nurses and the medical team are recommended to design and implement similar interventions to improve the HL of patients with IHD. Then the patients' self-care behaviors and treatment adherence might be improved.

Disclosures

Ethics Committee Approval: The study was approved at 2019-09-02, by the Ethics Committee of Kashan University of Medical Sciences (approval number: IR.KAUMS.NUHEPM.REC.1398.040).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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