

Influence of Health Literacy on Medication Adherence Among Elderly Females With Type 2 Diabetes in Pakistan

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Abstract

Health literacy is how well the patients are able to attain, deal with, and understand basic health information. This is particularly important when it comes to comprehending prescribed medication instructions. To improve the communication strategies for health-care professionals during patient counseling, our study aimed to assess the influence of health literacy and medication adherence in older patients. The objectives of the study were to evaluate associations that occur between the level of health literacy and medication adherence. This study used a convenience sampling method of females (older than 60 years) attending the diabetic clinic in two hospital settings ($N = 524$). All study participants filled three validated questionnaires: these were the Literacy Assessment for Diabetes, the Diabetes Numeracy Test, and a modified Brief Adherence Rating Scale. To assess the spectrum of health literacy differences, we used χ^2 analysis and linear regression analysis. Individuals with adequate health literacy were more likely to remember to take their medications compared with those with inadequate health literacy, $\chi^2(4) = 11.6$, $p = .04$. Adequate literacy level study participants were more likely to not change the dose of their medications without medical advice (12.3%) compared with those individuals with inadequate health literacy (2.8%), $\chi^2(4) = 11.13$, $p = .03$. The results in our study suggest that health-care professionals should focus on appropriate communication attuned to the assessment of health literacy levels particularly in older female patients when discussing medication instructions.

Keywords

health literacy, medication adherence, type 2 diabetes mellitus, older females, Pakistan

Introduction

Diabetes requires the persistent management of lifestyle aspects such as diet, exercise, glucose monitoring, and particularly medication to achieve the targets of glycemic control. Diabetic individuals are expected to closely mirror normal physiology using a variety of interventions.

Research suggests one of the greatest vulnerabilities in diabetes education is inadequate health literacy. Health literacy is how well the patients are able to attain, process, and understand basic health information regarding the management and control of their disease.¹ Of particular importance is comprehending instructions related to patients' prescribed medications.

Glasgow et al. developed a model that linked disease management and health-related outcomes to patients and the interactions they have with their health-care providers.² The factors that contribute to disease management include the duration of the disease, the complexity of the involved treatment, and the age of the patient. Elderly patients are

facing increasing challenges in the modern health-care environment due to the immense sophistication of medical procedures and therapeutic regimens. There is an increased demand for patient involvement in decision-making. Those such as the older adults, many of whom have inadequate health literacy skills, face the possibility of worse self-management skills, increased rates of hospital admissions, and issues with medication adherence.³

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The World Health Organization definition of adherence in chronic disorders is “the extent to which a person’s behaviour—taking medication, following diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider.”^{4(p17)}

Studies suggest that 55.6% of Type 2 diabetic patients in Pakistan report moderate adherence to medication.⁵

Health literacy goes beyond the skills of reading and writing (also termed print literacy). It also includes speaking or listening (oral literacy), conceptual knowledge, and the ability to apply numbers as needed to manage health (quantitative literacy or numeracy). Studies have suggested that it is an important independent predictor of health behavior and outcomes.⁵

Most patients with Type 2 diabetes mellitus (T2DM) require several different medications to help reduce disease-related complications. The benefits of treatment are hindered by a lack of medication adherence.

Health literacy and numeracy are considered to be related, and there are patients who have adequate health literacy but are deficient in basic numerical abilities.⁶ In emerging markets such as Pakistan, a very large proportion of patients have low incomes, wide discrepancies in the availability of education, and adequate health care with elderly females being particularly vulnerable. According to the United Nations Educational, Scientific and Cultural Organization, Pakistan at 55% has one of the lowest literacy rates in the world and stands 160th among world nations. The adult literacy rate for Pakistan is 65%, with males at 69% and females at 40%. Overall, the elderly population in Pakistan has a literacy rate of 38% which is significantly lower when compared with other age groups.⁷

The prevalence of diabetes in South Asia is higher in comparison to worldwide statistics, and in Pakistan, the prevalence of T2DM is 11.77%.⁸

We hypothesized that older females with inadequate health literacy are less likely to adhere to medication regimens due to incomprehension about disease-specific self-management tasks. Failing to comprehend the importance of the details of their medication regimens would lead to a lower incidence of implementing the correct self-management strategy.

The aim of our study was to evaluate the level of health literacy of older female patients with T2DM in Pakistan and the impact that this had on medication adherence.

Materials and Methods

Study Design and Study Participants

Our research was a cross-sectional survey based on a study that took place in two private sector hospital centers located in the same city—Lahore, Pakistan. The study participants included outpatient females older than 60 years with diabetes and concurrent cardiovascular disease. All participants were

on treatment regimens including combinations of insulin, oral glucose lowering medications such as metformin, sulfonylurea, and glibenclamide along with cholesterol- and blood pressure-reducing medications.

Exclusion criteria were any evidence of psychosis or dementia and the presence of any other current diabetic complication such as neuropathy, retinopathy, nephropathy, and chronic pain. We estimated these conditions alter medication adherence, and these particular patients face a variety of challenges in managing their medication regimens. For patients who had visual acuity of 20/50 or worse we used a Rosenbaum Screener (Prestige Medical, Northridge, CA) for exclusion. Visual acuity has a direct impact on literacy and numeracy due to the visual challenges involved.

We calculated our sample size,⁹ and based on this, we approached 600 patients who we identified from the clinic register. We used nonrandomized convenience sample selection. We were able to get 550 individuals to agree to participate but by the time the study actually began, 26 patients dropped out for reasons unrelated to the study.^{10,11} We eventually had a total of 524 participants in total from both centers who took part in the study.

Measures Used

Medications treatment groups were classified into three groups: oral blood glucose lowering, injectable blood glucose lowering, and oral cholesterol or blood pressure.

Participants had an hour in a single assessment session to complete the three sets of measures. Information on the socio-demographic characteristics and medication regimen were collected by the face-to-face interview. This aspect of our study used the qualitative research approach. Data for the other three instruments were collected by the following validated self-administered questionnaires: Literacy Assessment for Diabetes (LAD)¹² and Diabetes Numeracy test (DNT)¹³ for health literacy and Brief Adherence Rating Scale (BARS) for medication adherence was used.¹⁴

Health Literacy

This involved using the LAD. When using this instrument, the administering health-care professionals can better understand the patient’s health literacy levels. This assists health-care professionals for better approaches in giving nutritional and medical instructions.^{12,15} This instrument assesses the adult patient’s capacity to read medical terms, understand terms used that are for diabetes and also to interpret common nutritional information. In this test, study participants should pronounce 60 words, in 3 columns in the order of increasing complexity. For scoring, a plus (+) is given for each correctly pronounced word, a zero (0) for each mispronounced word, and a minus (–) for words that are not attempted. The raw score is the total of the three lists and this is then converted to a reading grade level; 0 to 20 is as

fourth grade and below, 21 to 40 is fifth to ninth grade level, and 41 to 60 are ninth grade and above.¹²

The DNT is another valid assessment tool that is specific for diabetic numeracy. This test evaluates a variety of quantitative skills used for common diabetes tasks such as appraising a nutrition food label, calculating requirements for medication and also for understanding what the results mean from the self-monitoring of glucose.^{13,16} The DNT also has word problems that assess calculation, interpretation of tables, graphs or figures, and the application of required numeracy skills to solve problems and to perform self-management tasks that are specific to diabetes care.¹⁷

Medication Adherence

The BARS test is a valid and reliable tool used to assess medication adherence. It has three questions that inquire about the patient's knowledge of their own medication regimen and episodes of when taking medication have been missed. It asks patients about the number of prescribed doses of medication per day, the number of days in past month when the patient did not take the prescribed doses, and the number of days in the past month when the patient took less than the prescribed dose. The key measure of adherence is by using the visual analogue scale to assess the proportion of doses taken by the patient in the past month (0%–100%). The test has good sensitivity (73%) and specificity (74%).¹⁸ There are several other tests available but we selected this particular test due to time constraints when using several tools within the hospital setting.¹⁹

Urdu is the national language of Pakistan, so the three questionnaires used in this study were translated using the back-translation method. The questionnaires were translated to Urdu by one qualified translator and then translated back into English by an independent qualified translator who was blinded to the original questionnaires. The two source language versions were compared and a consensus was reached. For the LAD, DNT, and BARS tests, the Cronbach's α measuring internal consistency was calculated to be .81, .85, and .83, respectively. The reliability coefficients were .76, .82, and .84, respectively. These values indicate that the Urdu versions of the three questionnaires are consistent and reliable enough to be used for this population.

Sociodemographic Characteristics, Health Status, and Medication Regimen

Participants were asked their age, annual income, education obtained, age of diagnosis (length of time since they have been diagnosed) of diabetes, presence of diabetic complications, and the list of medications used for diabetes. Glycemic control was appraised by obtaining the most up-to-date glycosylated haemoglobin (HbA1C) value from their hospital medical records.

Participants identified their diabetic medications and the doses they were using in the prior month. The study participants were also asked to identify their medications from a chart. This chart illustrated the most common types of diabetic medications that are widely used in Pakistan. Individuals pointed out to the medications that they were taking and mentioned their doses. The interviewer would record their answers, cross checking with the initial verbal response.

For this study, we used a modified BARS for diabetes to assess medication adherence. This is a validated self-report medication adherence measure that is commonly used in outpatient settings.¹⁴

Items that were included as follows: (a) How many days in the past month did you not take your prescribed medication doses? and (b) How many days in the past month did you take less than the prescribed dose?

For the number of days, the options were as follows: few (rarely; <7), (often) 8–13, (frequently) 14–20, and most (mostly) >20.^{14,18} For taking less than the prescribed doses, the options were always or almost always, usually, sometimes, and never or almost never.²⁰

Procedures

Women older than 60 years were recruited from the outpatient diabetic clinic of the private sector Punjab Care hospitals in the city of Lahore, Pakistan during the time period from January 2018 to February 2019. Research staff involved in the study were trained on the eligibility criteria of the study, pinpointing the individuals who could take part in the study, administering the questionnaires, scoring and recording the results accurately. The trained research staff then used the diabetic clinic roster to identify eligible patients and then talked to them in the clinic waiting room about the study. The study participants unable to read the self-administered surveys were interviewed by trained research staff so as to fulfill all study measures.

Approximately, 600 patients were approached with only 550 who agreed to participate. By the time the study actually began, 26 participants dropped out for reasons that were unrelated to the study and we eventually had a total of 524 participants who took part in the study.

Data Analyses

For statistical analysis, we used Package for Social Science (SPSS) Version 23 (SPSS Inc., Chicago IL). The aspects of medication adherence that we focused on were the following: not remembering to take medications, medication dose alteration, halting medication, deliberate missing a dose, and self-reduction of medication. We tested the bivariate association between these aspects of medication adherence using χ^2 analysis. To test the association between health literacy (LAD score or DNT score) and additional factors (education, income, and health status) that could influence medication

adherence score, we used linear regression. A p value of .05 was used. We performed preliminary analyses to ensure there was no violation of the assumption of normality and linearity. The classification for self-reporting of each individual's health status had the categories: excellent, good, fair, or poor. Measures that were assessed as continuous variables included the number of medications prescribed and the number of medications being currently taken. By extrapolating the scoring of standardized LAD and DNT, the participants were divided into those who had inadequate health literacy (score < 85%) and those who had adequate health literacy (score > 86%). The contingency table was used to compare between the adequate and inadequate literacy groups.

Results

Sociodemographic Characteristics, Health Status, and Medication Regimen

The mean age of the 524 study participants was 64 years. The average duration of the patient having been diagnosed with diabetes was 7 years \pm 2.5. Details of the demographic and medication history are summarized in Table 1.

Most study participants were married (413, 78.6%), with an annual household income of \$10,000 or less (414, 79%). A large proportion of participants self-reported that they were experiencing fair or poor health (277, 51.1%). Most participants had education levels that ranged from high school (20.2%) or less (270, 51.5%). Participants were prescribed an average 4.3 number of medications and were consuming an average number of medications which was 4.6. The higher number of consumption of medications included over the counter drugs and self-medication could be due to unaffordability and limited access to medical care.

Participants had their health literacy frequencies calculated. Table 2 shows the details of the three questionnaire results. The average LAD score was 52.0 out of a total 60.0 (standard deviation [SD] = 12.4). For the DNT score, the median (interquartile range) was 63% (41%–82%). This meant that the majority of the participants (66.2%) had adequate health literacy levels. Based on the LAD and DNT scores, we classed the participants as those who had inadequate health literacy levels ($N=210$, 40%) and those who had adequate health literacy levels ($N=300$, 57.2%).

The average adherence score was 3.1 out of a possible 5 ($SD=0.5$). Using the literature, we classed the responses for number of days as rarely (few < 7), often (7–13), frequently (14–20), and mostly (most > 20). For taking less than the prescribed doses, the options were always or almost always, usually, sometimes, and never or almost never.

The χ^2 analysis of the relationship between medication adherence and health literacy is presented in Table 3. The table highlights the connections between the participants' health literacy levels to medication adherence in the detailed

Table 1. Details of the Demographic and Medication History.

Variable	N or mean (%)
Age	64
Marital status	
Single	25 (4.7)
Married	413 (78.8)
Widowed	54 (10.3)
Divorced	15 (2.8)
Separated	17 (3.4)
Education completed	
No education	85 (16.2)
I to II grade	270 (51.5)
High school graduate	106 (20.2)
Vocational training	48 (9.4)
College degree	15 (2.8)
Annual income	
\$10,000 or less	414 (79.1)
\$10,001–\$20,000	86 (16.4)
No answer	24 (4.5)
Health status	
Excellent	89 (16.9)
Good	118 (22.5)
Fair	48 (9.1)
Poor	269 (51.3)
HbA1c values (%)	9.9 \pm 5.1 (SD)
Prescribed number of medications (average)	4.3
Number of medications taking (average)	4.8
Medication adherence score (average)	3.1

Abbreviations: SD , standard deviation; HbA1c, glycosylated haemoglobin.

Note. Total $N=524$.

sections (days not taken the medication and days taking less than prescribed dose of medications).

Individuals with adequate health literacy had fewer days of skipping medications (48.6%) compared with those with inadequate levels of health literacy, $\chi^2(2) = 11.6$, $p = .04$.

Participants with adequate literacy levels were more likely to state they did not take less than their prescribed dose (53.3%) compared with those with inadequate health literacy levels (2.8%), $\chi^2(2) = 11.13$, $p = .02$ (Figure 1).

There were no significant associations between health literacy (LAD or DNT scores), additional factors (education, income, and health status), and medication adherence score. These results are not shown.

Discussion

Health literacy is a term that is often used to study populations in developed countries and in several developing countries. In frontier markets such as Pakistan, however, this is an often overlooked field of study. The country continues to struggle with low health literacy levels that lead to later disease stages at diagnosis, low treatment adherence rate, and a lack of understanding about the concepts of health and the prevention of disease.²¹ This is due to an inadequate health-

care infrastructure in combination with high illiteracy levels. Older females in particular have fewer opportunities to education and obtaining or enhancing literacy skills.^{22,23} In our study, we found 355 (67.7%) of our study participants with no education or less than high school education and this is what we expected to find. There are several potential factors

that could lead to inadequate health literacy in older females in frontier markets such as Pakistan (Figure 2).^{24,25}

Studies in other countries have demonstrated poor adherence rates of medication among diabetics and patients who are suffering with other chronic conditions.²⁶ There have been numerous studies from around the world that assessed the impact of medication adherence on patient outcomes with diabetes. An observational study based in United States correlated high medication adherence levels in diabetics with an overall reduction in health-care costs, and another study showed lower adherence levels led to higher all-cause hospitalization and all-cause mortality.^{27,28} Adherence to medication in diabetes is therefore of utmost importance, and specific aspects of lower medication compliance should be identified to provide targeted health-care policy. Studies such as Iqbal et al. and Nazir et al. held in Pakistan have focused on health-related quality of life in relation to medication adherence.^{29,30} There are also a few studies with varying designs and results that shed light on adherence to blood glucose lowering medications in older patients with T2DM.^{22,31} These are very vital aspects of medication adherence when it comes to diabetics. However, in our study, we chose to focus specifically on the influence of health literacy on medication adherence among elderly females with T2DM and concurrent cardiovascular disease in Pakistan. To our knowledge, this is the first hospital-based study for evaluation of this relationship.

The study by Iqbal et al. assessed medication adherence in patients from 18 years age and above, including both genders.⁵ We targeted older females because we hypothesize that older male patients do not have the same issues as older female patients because of the prominent presence of gender bias in the South Asian region.³²

Inadequate health literacy levels predisposes issues with reading medication labels, interpreting blood glucose levels, following medication schedules, comprehending

Table 2. Detailed Results of the Literacy Assessment for Diabetes, Diabetes Numeracy Test, and Brief Adherence Rating Scale Scores.

Test and scores	N (%) Total N = 524
Literacy Assessment for Diabetes	
0–20	25 (47)
21–40	413 (78)
41–60	54 (10)
Brief Adherence Rating Scale	
How many days in the past month did you not take your prescribed medication doses?	
<7	21 (4)
8–13	385 (73)
14–20	89 (16)
>20	29 (5)
How many days in the past month did you take less than the prescribed dose?	
Always/almost always	49 (9)
Usually	357 (68)
Sometimes	89 (17)
Never/almost never	29 (5)
Diabetes Numeracy Test	
% correct	
Domain	
Nutrition Q1–9	52.5
Exercise Q10–13	62.9
Blood glucose monitoring Q14–17	71.5
Oral medications Q18–22	69.1
Insulin Q23–43	49.9

Table 3. χ^2 Analysis of the Relationship Between Medication Adherence and Health Literacy.

Variable	Inadequate health literacy N = 210 (40%) N (SD)	Adequate health literacy N = 300 (57.2%) N (SD)	Total N = 524 N (SD)	p
Days that medication was not taken?				
Rarely	36 ± 12.3	146 ± 18.6	176 ± 15.4	0.04
Often	28 ± 13.3	58 ± 14	86 ± 8.6	
Frequently	44 ± 11.7	49 ± 13	93 ± 12.3	
Mostly	102 ± 29.5	47 ± 13.6	149 ± 21.5	
Days taking less than prescribed dose?				
Always/almost always	32 ± 10.4	16 ± 4.6	48 ± 7.5	0.02
Usually	60 ± 19	12 ± 4	46 ± 11.5	
Sometimes	66 ± 10.1	112 ± 3	76 ± 6.5	
Never/almost never	52 ± 24.7	160 ± 28	136 ± 26.3	

Abbreviation: SD, standard deviation.

Note. The χ^2 analysis results that were used to assess health literacy level differences in the medication adherence sections (days not taken the medication and days taking less than prescribed dose of medications).

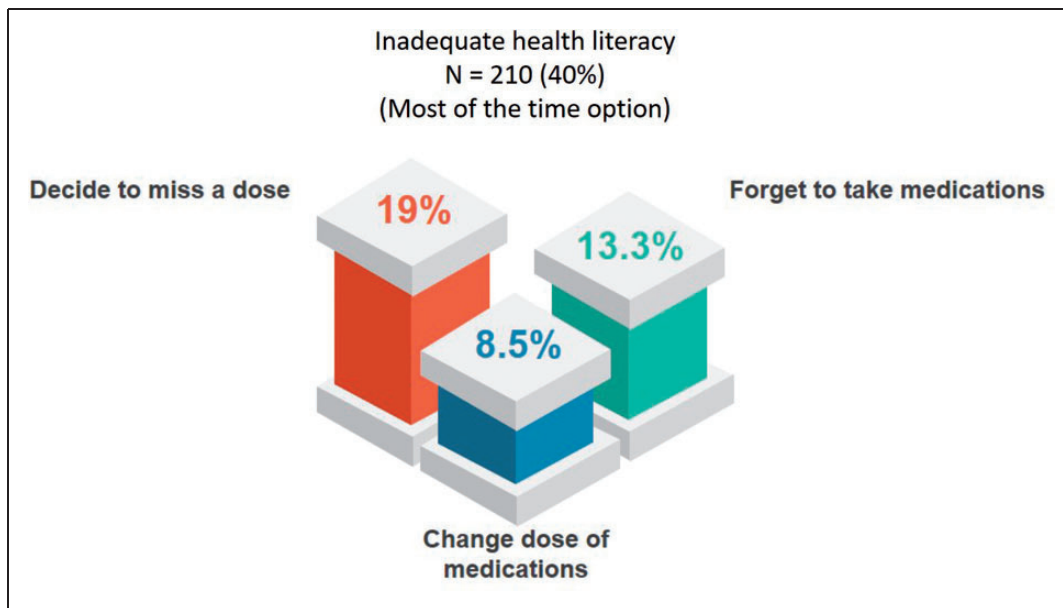


Figure 1. Inadequate health literacy results.

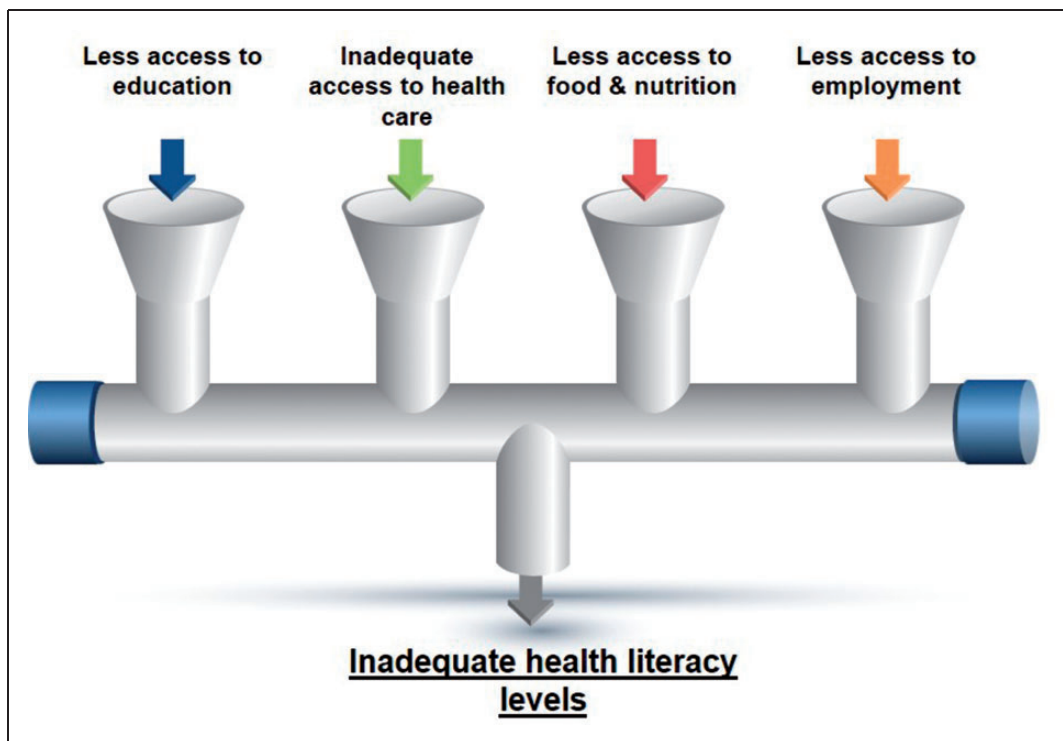


Figure 2. Potential factors that could play a role in adequate health literacy in older females in Pakistan.

appointment notifications, and informed consent documents.^{33–35} The appropriate processing of oral communication evaluating medical risks and access to health care are also affected.^{36–38}

Due to the wide variation in health literacy and its subsequent consequences, individuals with low levels of health

literacy are ill equipped to manage their chronic disease right from the stage of initial diagnosis.³⁹

Appropriate diabetic care requires complicated pharmacological regimens and our participants were prescribed an average number 4.3 of medications and were consuming an average 4.6 number of medications. The higher number of

consumption of medications included over the counter drugs and self-medication due to unaffordability and access to medical care. Polypharmacy brings about its own issues in the older age and increases the already vulnerable population risks for falls, declining cognitive functions, hypoglycemia episodes, and inadequate pain relief.⁴⁰

Diabetic patients experience greater difficulty in comprehending the risks and complications associated with their disease. Research suggests that pharmacotherapy adherence is vital for glucose control in diabetics and is directly related to patient self-management of diabetes. This means the differences in these aspects of managing diabetes are associated with variability in the outcomes of treatment.⁴¹

Although many studies have focused on identifying non-health literacy influences on medication adherence, this study focused on highlighting the association between health literacy and specific aspects of medication adherence.¹⁵

Medication nonadherence is a prevalent and costly problem among T2DM patients.⁴² Studies estimate that approximately one in three diabetic patients do not take their medications as prescribed.⁴³ Higher rates of nonadherence differ with race, ethnicity, and socioeconomic status.^{44,45} Nonadherence to medication is associated with severe complications such as myocardial infarctions, stroke, and a higher risk of associated mortality.^{46,47} Understanding the critical aspects of where effective interventions would be most effective are important to address nonadherence issues.^{48,49}

Medication adherence is a key factor when considering chronic disease therapy in older people.^{50,51} As age increases, medication adherence and beliefs in medicines alter.⁵²

A large proportion of participants 277 (51.1%) self-reported experiencing fair or poor health that matches other regional-based studies.²¹ Our study focused on female participants and there are studies that show gender differences are noticeable when self-reporting health status especially in chronic conditions.⁵³ Considering lower scores in several aspects of those with inadequate health literacy levels, the self-reporting of poorer health could be due to suffering from poorly controlled diabetes and its associated complications that accompany diabetes such as depression and chronic pain that affect the quality of life and the health status of individuals.⁵⁴

In terms of glycemic control, the HbA1c values of most of the study participants were above target (9.9 ± 5.1). This is in line with the proportion of study participants with medication adherence issues and also goes with other studies.^{55,56} Glycemic control is the cornerstone of diabetes therapeutic regimens. The quality of life, injuries such as fractures, microvascular, and macrovascular complications are all affected by appropriate control of blood glucose levels.⁵⁷⁻⁶⁰

There are other questionnaires available to assess literacy in diabetic patients.^{15,61-63} However, many of these are hampered with issues ranging from complexity, interpretive errors, and administering to patients in a real-world clinical

settings.⁶³ The assessment of health literacy specifically in diabetic individuals can utilize established tools such as the LAD and DNT.^{12,13} The main finding in the study is that health literacy, in the form of LAD and DNT scores, is a positive determinant for medication adherence. This study also highlighted very specific aspects of medication adherence that differ by health literacy level, for example, forgetting to take the medications, deciding to alter the dose of medications, and deciding to skip doses.

Our study identified that approximately 40% of participants had inadequate levels of health literacy that is in line with other studies.^{64,65} Inadequate health literacy meant reading at a level below that of ninth-grade level, and this leads to challenges in reading and comprehending patient education materials especially those containing vital instructions for prescribed medications.⁵¹

A large percentage of study participants with inadequate literacy levels often had days when they missed taking their medication. Research suggests that older adults have more difficulties in managing their medication regimens,⁶⁶⁻⁶⁸ but these studies have not focused on the impact of health literacy on the medication adherence.

Our research suggests that there is a significant difference in individuals having adequate health literacy versus those who have inadequate health literacy in specific aspects of medication adherence; not taking medication and altering the medication dose.

While these findings help to shed light on the gaps in knowledge about health literacy in medication adherence for the older female T2DM adult, there is a clear need for future studies to confirm these findings on a much larger scale. Identifying those patients with inadequate health literacy scores could pave the way for implementing effective diabetes educational programs that are specific to a patient's unique needs⁶⁹ and stress on the importance of effective health-care communication across a variety of health-care professionals that patients come across.⁷⁰

Conclusions

Elderly female patients with T2DM are a particularly vulnerable group to having low health literacy. Our study showed that there is a significant difference between individuals with adequate levels of health literacy and those with inadequate health literacy. These differences have a significant impact on medication adherence. The most significant findings in medication adherence issues were found to be skipping medication doses and altering medication doses without health professional consultation.

Lower health literacy levels and poor numeracy skills have been linked to challenges such as glycemic control, self-efficacy, self-care behaviors, and medication adherence when it comes to diabetes. Our study showed that above target HbA1c, one of the key indicators of glycemic control, was significantly associated with lower health literacy levels.

Confronting the issue of literacy in diabetes educational and management programs that are multidisciplinary has the potential to influence and improve important health outcomes. Despite the importance, there are still large gaps in the knowledge about the impact of a variety of strategies in improving health literacy including those for patients and health-care providers. Inadequate diabetes-related numeracy is a potentially modifiable barrier toward successful disease management. It is important to developing educational programs and specific adaptive tools specifically designed to improve effective health-care professionals' communication toward older patients with inadequate health literacy levels. More institutional support is required to improve the interactions and communications between particularly vulnerable patient groups and health systems, since health literacy is vital to optimize delivery of diabetes care and achieve target glycemic control.

Limitations of Study

The limitations of this study include the small size used in the study. The study sample was from two hospital settings which can have an effect on generalizability and population bias error. Using convenience sampling has its own issues with sampling bias and that the sample is not representative of the entire population. The LAD, the DNT, and a modified BARS are popular, easy, and economical methods of data collections. However, this method of data collection has limitations because it does not account for physical ability, means of transport, known modes of communication, and so on. The outcome of these questions can be biased by patients supplying false information.¹⁴

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Authors' contribution

Conceptualization and supervision were by N. H. A. S. A. S. contributed to the methodology and formal data analysis. Both N. H. and A. S. A. S. were responsible for the writing—original draft preparation, review, and editing.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics

Ethical approval was provided by the Punjab Care hospitals review board (Approval no. 38928). The study was conducted in a two clinical centers in agreement with the ethical guidelines of the Declaration of Helsinki, Good Clinical Practice guidelines, and applicable regulatory requirement. Participants provided informed consent in accordance with Institutional Review Board of the

Punjab Care hospital guidelines. Participants were made aware that all data would remain anonymous.

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