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RESEARCH ARTICLE

Assessment of Alternative Medicine Use, Costs, and Predictors of Medication Adherence among Diabetes Mellitus Patients in Palestine

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Abstract: ***Background*:** Diabetes Mellitus (DM) is considered the fourth leading cause of death in Palestine, with a prevalence of 9.1% in patients aged 20-79 years, and has increased to 20.6% in 2020.

***Aims*:** This study aims to estimate DM costs, compare DM total health care cost among patient characteristics and DM management (*e.g.* anti-diabetic medications and alternative medicine), as well as assess MA and its predictors including patient characteristics, DM management, alternative medicine use, and DM costs.

***Methods*:** A cross-sectional study was conducted for the past one year among 479 diabetic patients, selected by convenience sampling and snowball sampling methods *via* electronic post of an online questionnaire, including a web link to the questionnaire page in a Google Form *via* email or public social media pages and applications. Data on patients' socio-demographic and clinical characteristics, medication profile, use of medicinal plants as alternative medicine, costs, and Medication Adherence (MA) were collected. The Statistical Package for Social Sciences (SPSS v. 25) was used to perform a descriptive, Kolmogorov-Smirnov test, univariate analysis, Mann-Whitney or Kruskal-Wallis test, multiple linear regression, binary logistic regression, and multiple logistic regression analysis. A p-value < 0.05 was considered statistically significant.

Results: More than half of the participants were male and living in villages (50.7%, 59.1%, respectively). Approximately 51.4% received Oral Hypoglycemic Drugs (OHDs) and only 16.1% received insulin. The participants receiving ≤3 medications daily acquired the highest percentage (55.7%), and less than half received medicinal plants as an alternative medicine for the management of DM. The estimated total DM health care cost per year incurred by patients and family members was Israeli Shekel 988,276 (US Dollar 307,590). More than half of the participants were considered adherent with the Eight–Item Morisky Medication Adherence Scale (MMAS–8) score ≥6. It is noteworthy that the use of alternative medicine was significantly associated with total health care cost and MA. Furthermore, DM duration was significantly associated with MA. These results are worth taking into consideration.

***Conclusion*:** This study reflects the need for strengthening the patient-health care professionals' relationship, and to enhance the role of preventive education, and the importance of awareness about MA, DSCMBs, and the use of alternative medicine based on evidence-based strategies to improve MA, glycemic control, meanwhile reducing the costs incurred by patients and family members.

Keywords: Medication adherence, alternative medicine, type i diabetes, type ii diabetes, hypertension, dyslipidemia.

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1. INTRODUCTION

Diabetes Mellitus (DM) is a common health problem with medical consequences effecting economic and social genic genetic factors as well as non-genetic factors that result consequences for patients, health care providers, and societies [1, 2]. It is a multifactorial disease caused by oligo- and poly form a lack of balance between energy intake and output and other lifestyle-related factors. It is one of the world's fast-growing chronic diseases with a prevalence estimated to be 108 million in the year 1980 and 422 million in the year 2014 and will increase to 700 million cases by the year 2045 [3]. Several studies have proven that the estimated DM world health care expenditures were at least USD 376 billion in 2010, and will be USD 490 billion in 2030. Thus, DM care costs have been increasing over the years and will continue to increase. The health care cost of DM varies by region, developed and

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developing countries, age, gender, income levels, and other factors [4].

The developing countries accounted for the largest share of the economic burden of DM, of which 75% of these estimates could be attributed to an aging population, unhealthy diet, obesity, increasing urbanization, sedentary lifestyle, and rapid social changes [5]. Multiple medications are often prescribed for the management and treatment of DM and its associated conditions include diabetic complications such as retinopathy and nephropathy and non-DM-related comorbidities such as hypertension, dyslipidemia, and cancer [6].

Diabetes Mellitus and its complications result in an increasing economic burden on patients, health care providers, and communities. Subsequently, the benefits of Diabetes Self-Care Management Behaviors (DSCMBs) including Medication Adherence (MA) are evident, often associated with better health outcomes represented by better glycemic control, lower diabetic complications, lower hospital admissions, lower costs, and mortality rates [7]. In contrast, it was indicated that DM patients who were non-adherent to prescribed medications (*i.e*., low MA scores) were found to be in poor glycemic control (*i.e*. HbA1c >7%), which resulted in the development of diabetic complications, higher blood pressure, and higher serum cholesterol and triglycerides concentrations. Therefore, the sharp rise in DM health care costs is mainly attributed to managing diabetic complications, especially when hospitalization and inpatient health care are needed [8].

Furthermore, patient DSCMBs in general and MA, in particular, were found to be significantly associated with nonmedical costs (*e.g*., transportation costs) and medical costs (*e.g*. medication costs). Therefore, good glycemic control can be achieved by DSCMBs, which constitute MA as one of its most important pillars and a part of the World Health Organization (WHO) and the Palestinian guidelines for DM management. In addition, MA is believed to be influenced by factors beyond the traditional socio-demographic and clinical characteristics [9].

The majority of DM patients require a long–term administration of OHDs and insulin to ensure good glycemic control [10]. Moreover, the phenomenon of alternative medicine use for chronic diseases in general and DM, in particular, has also spread among DM patients as an important and complementary treatment to traditional treatment (*i.e*., OHDs & insulin). Alternative medicine has been defined as a caring approach, including the use of medicinal plants [11]. Although much is known about the adverse downstream effects of medication non-adherence, the determinants of MA are less well defined. Most studies have looked at either individual-level or system-level factors independently, whereas few studies have used large generalizable cohorts. This suggests that there is a complex model of socio-demographic, clinical characteristics, drug utilization pattern, DSCMBs, and glycemic control that will be finally related to DM costs for patients, health care providers, and communities [12].

The foundations for DM management have been regulated by WHO, which recommends all ministries of health registered in WHO to implement its guideline for DM diagnosis and management. In addition, efficient resource utilization is required. Several studies were carried out in Palestine about DM. However, none of these studies assessed the relationship between factors such as alternative medicine use, cost, MA, and glycemic control. The oral hypoglycemic drugs used to treat type II DM are Insulin stimulators; they stimulate Insulin secretion by β–cells, which in turn are subdivided into Sulphonylureas and Non–Sulphonylureas such as Glibenclamide and Repaglinide, respectively. Insulin sensitizers increase Insulin sensitivity and are subdivided into Biguanides (Metformin) and Thiazolidinediones. The available anti-diabetic agents in the Palestinian Drug Formulary are Insulin, Glibenclamide, and Metformin, as recommended by WHO [13-15]. In addition, the use of herbals as an alternative medicine for DM management has become somewhat acceptable among DM patients. Cinnamon and Fenugreek were most prominently used as alternative medicines for DM management worldwide. Moreover, herbals play an important role in the treatment and management of DM and other chronic diseases in Palestine [16].

The scarcity of research and data concerning DM costs and MA in Palestine highlights the importance of determining expenditures borne by patients, family members, health care providers, and communities that might provide decision-makers with the necessary information to further aid in developing personalized DM management and controlling strategies. Moreover, a new and creative idea concerning alternative medicine use for DM management, which will form a future basis for evaluating the impact of its use on other health outcomes of DM health care needs to be added [17]. Subsequently, this study was conducted among DM patients in Palestine to estimate DM costs (*e.g*., direct costs), compare DM total health care costs among patient characteristics and DM management (*e.g*. Anti-diabetic medications and alternative medicine), as well as assess MA and its predictors including patient characteristics, DM management, alternative medicine use, and DM costs.

2. MATERIALS AND METHODS

2.1. Study Design

This study was cross-sectional and was conducted including DM patients in Palestine. Diabetes Mellitus costs to patients were estimated for a given period extended for one year. Costs incurred by patients and family members were estimated based on co-payments for insured patients and/or fees for uninsured patients and production losses. Data sources used in this study were a set of socio-demographic and health information sections, cost diary, and Morisky Medication Adherence Scale 8-items (MMAS-8) which were conducted *via* an online questionnaire, and co-payment and/or fees lists.

2.2. Study Participants

This study employed patients who met the sampling criteria from an accessible population who visited health care centers serving DM patients. Subsequently, the study included: 1) patients diagnosed with DM; 2) received ongoing anti-diabetic treatment; 3) currently under active DM health care within the previous one year, and 4) willing to participate in the study without physical and/or mental conditions that could interfere with their ability to complete data collection

requirements. Convenience sampling and snowball sampling methods were used to reach participants. The sample size was calculated based on a single proportion formula, considering a sample proportion of 50% while using a cross-sectional study design wherein n = required sample size (n = Z (α/2) 2 pq/d2) and 95% C.I with a 5% margin of error. Therefore, a minimum sample size of 385 was required as the study's target population to represent the general population. Subsequently, complete data were collected from 479 DM patients.

Participants were recruited by electronic post of an online questionnaire, including a web link to the questionnaire page in a Google Form *via* email or public social media pages and applications (*e.g*., Facebook, WhatsApp, *etc*.). The participants could answer the electronic questions, submit which re-upload the answers in the same electronic form back to the researchers. Patients excluded from the study were those who refused to participate, without social media access or telephone, and did not meet the sampling criteria. The study was approved by the Institutional Review Board (IRB) of An-Najah National University in Nablus (West Bank of Palestine) with a reference number of Phr/05/2015 and was performed in compliance with the Helsinki Declaration for research in humans. All participants provided their informed consent to participate in this study before they were included.

2.3. Data Collection

The participants were asked to complete online questionnaires to collect data concerning age, gender, marital status, occupation, additional chronic diseases, Body Mass Index (BMI), smoking status, anti-diabetic treatment modalities, alternative medicine, and others. Participants were asked about their weight and height to calculate their BMI, which was calculated as weight in kilograms divided by height in meters squared. Participants were required to record resource use in a detailed way to allow cost calculation by multiplication with unit prices and/or unit costs. The cost diary was used in the online questionnaire to cover visits to DM health care centers during the past year and as a tool contributing to assessing costs of different kinds. The participants were required to record information concerning cost analysis.

Direct medical costs are an impact of DM health care on health care services use such as general practice visits, specialist care, lab tests, and unit prices of medication doses. The cost diary's contribution to the direct medical costs measurement is through the visit number recorded by participants *via* the online questionnaire; finding out who incurs the costs, whether the participant or any of his/her family members, friends, or others and thus the overall distribution costs; and medical service/s received and thus confirmed or denied copayments/fees payment [18]. Data concerning direct non–medical costs represented by transportation ways and costs were collected. The participants were asked about whether his/her visit was accompanied by someone or alone, and with this part, a complete calculation of the total transportation costs per visit according to the transportation mode used to arrive at the center could be made [19, 20].

Time loss costs refer to calculating the number of days/hours absent from paid and/or unpaid work and days lost from housekeeping and other daily activities mentioned by the participants during each visit [21]. Based on their occupation, the participants were asked about the number of days and/or hours that he/she took as leave, seeking to go to the clinic during the past year. The same thing applied to employed persons accompanying the participant to be able to estimate the time lost costs per visit. Hence, the total time loss costs during the past one year were calculated to get a complete picture of work absence/normal activity lost days/hours of the participants. Furthermore, the participant was directed to indicate the arrival time to the clinic, distance traveled, and time needed to arrive at the center. Total health care cost was estimated by collecting costs that account for the total direct medical costs; as well as total direct non–medical costs and total time loss costs.

Medication adherence was measured using MMAS–8 [22, 23]. This scale consisted of eight items. The first seven items are yes/no questions while the last eight questions are answered on a five-point Likert scale, eight scores from the highest score of MMAS–8, so the scores can range from zero to eight. One score is given for each "No" answer except for question number five where one score is given for "Yes" answers. In the eighth question, zero scores are given if the answer is ticked to "all the time" items, in contrast to "never/rarely" answers where one score is given. Therefore, the total MMAS–8 score is the sum–up of the scores for the eight items. All prescribed medications were abstracted from the participants by the online questionnaire. Participants' responses were treated with confidentiality.

2.4. Statistical Analysis

Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS v.25). The Kolmogorov-Smirnov test was used to assess DM costs and total health care cost for normality. Subsequently, they were found to be non-normally distributed. Consequently, median (inter-quartile range: Q1-Q3) Total health care costs were calculated for subgroups of participants based on categorical variables related to patient characteristics, DM management (*e.g*. medications), and alternative medicine profiles, assessed for statistical significance using nonparametric tests including either Mann–Whitney or Kruskal-Wallis test, and followed by multiple linear regressions. Furthermore, intergroup differences in median (inter-quartile range: Q1-Q3) DM costs and total health care costs were calculated for subgroups of participants based on MA. Subsequently, binary logistic regressions followed by multiple logistic regressions were conducted to determine factors and DM costs associated with MA. A p value < 0.05 was considered statistically significant.

3. RESULTS

3.1. Socio-Demographic & Clinical Characteristics of the Participants

Data for a total of 479 participants were analysed. The socio-demographic characteristics of the participants are summarized in Table **1**. The study demonstrated that the age category of >58 years old accounted for the highest percentage (40.9%), and more than half of the participants were

Table 1. Total health care cost among participants' socio-demographic characteristics (ILS at 2020 Prices).

Variable	Frequency (%)	Health Care Cost Median (Interquartile Range)	*p*-Value
Age:			
18-27	86 (18%)	594.5 (215.8-1589.3)	
28-37	15 (3.1%)	1123 (454-2392)	
38-47	41 (8.6%)	1074 (459.5-2342.5)	0.001
48-57	141 (29.4%)	1182 (599-2214.5)	
≥58	196 (40.9%)	1250 (631.3-2413.5)	
Gender:			
Female	236 (49.3%)	1123 (532.3-2298.8)	0.326
Male	243 (50.7%)	1074 (450-2217)	
Marital Status:			
Married	331 (69.1%)	1178.5 (567-2409)	
Separated/Divorced	4 (0.4%)	1059 (410.3-3603.8)	0.000
Single	91 (19%)	592 (219-1585)	
Widowed	53 (11.1%)	1182 (602-2090)	
Income Level:			
<2000	124 (25.9%)	1182 (472.5-2415)	
2000-4999	256 (53.4%)	1112.5 (482.9-2215.8)	0.584
5000-9999	78 (16.3%)	1044.5 (467.5-2254)	
≥10000	21 (4.4%)	736 (433.5-2026.3)	
Educational Level:	48 (10%)		
Literacy Study	219 (45.7%)	1329.5 (716.4-3478.5)	
Middle & High School		1378 (666-2412)	0.000
University Study	189 (39.5%)	845 (259-2029)	
Post Graduate Studies	23 (4.8%)	1144.5 (670-1833)	
Employment Status:	127 (26.5%)		
Home Duties	80 (16.7%)	1347 (666-2365)	
Own Businesses	57 (11.9%)	1117 (542.3-2382.8)	
Private Sector Employee		736 (262-1953.5)	0.079
Public Sector Employee	51 (10.6%)	1172 (494-2064)	
Retired		1135 (671.8-2625)	
Unemployed	38 (7.9%)	944.5 (252-2229.8)	
	126 (26.3%)		
Residency Place:	24 (5%)	979.5 (434.6-2241)	
Palestinian Refugee Camp			0.025
City	172 (35.9%)	1007 (409.3-2005.8)	
Village	283 (59.1%)	1142 (545-2416)	

males (50.7%). Furthermore, more than two-thirds of the participants (69.1%) were married, and the household monthly income range of 2000-4999 ILS acquired the largest percentage of the participants (53.4%). Middle and high school participants divested the highest proportion (45.7%). In addition, more than half were living in villages (59.1%) and less than half (35.9%) were living in cities. It is also noted that unemployed participants and those who indicated that their employment status was home duty made up the largest percentages of the participants (26.3% & 26.5%, respectively).

Concerning the clinical characteristics (Table **2**), the majority reported that they were diagnosed with Type 2 DM (70.4%), and those who were diagnosed with DM (*i.e*. DM

duration) for 1-7 years accounted for the highest percentage (47.6%). Moreover, less than half of the participants had 3 or more diabetic complications (40.7%), and more than half reported that they did not suffer from non-diabetic comorbidities (61.6%). Furthermore, the majority of the participants were non-smokers (76.2%). In addition, the distribution of the participants according to their BMI was: underweight (2.1%), normal weight (26.1%), overweight (38.8%), and obese (33%). Only 16.1% of the participants received Insulin, and more than half were receiving OHDs (51.4%), and less than a quarter received combination treatment with OHDs and Insulin (22.1%) for DM management. Furthermore, 203 participants stated that they received herbal products as alternative medicines for DM management (42.4%), and more than half took ≤ 3 medications daily (55.7%).

Table 2. Total health care cost among participants' clinical characteristics (ILS at 2020 Prices).

Variable	Frequency (%)	Health Care Cost Median (Interquartile Range)	*p*-Value
Type of DM:			
Type 1	142 (29.6%)	1061 (328.5-2220.3)	0.264
Type 2	337 (70.4%)	1123 (494-2281.5)	
Diabetes Duration:			
1-7 years	228 (47.6%)	1062.3 (474.8-2190)	
8-14 years	126 (26.3%)	1040 (352.5-2213.3)	0.669
15-23 years	73 (15.2%)	1432 (675-2610.5)	
≥ 24 years	52 (10.9%)	1135 (620.3-2486.3)	
Smoking:			
No	365 (76.2%)	1178.5 (536-2358)	0.910
Yes	114 (23.8%)	952 (260-2088.3)	
BMI:			
Underweight	10 (2.1%)	884.5 (180.1-1301.5)	
Normal	125 (26.1%)	845 (259-2184.5)	0.170
Overweight	186 (38.8%)	1065.5 (453.3-2212)	
Obese	158 (33%)	1362.5 (719.5-2455)	
Diabetic Complications No.			
0	107 (22.3%)	1014 (300-2116)	
1	93 (19.4%)	908 (408-1976.5)	0.055
2	84 (17.5%)	1607 (474-2718)	
≥3	195 (40.7%)	1163 (604-2362)	
Non Diabetic Comorbidities No.:			
0	295 (61.6%)	1048 (417-2124)	
1	149 (31.1%)	1142 (491.5-2289.5)	0.209
2	31 (6.5%)	2412 (767-4070)	
≥3	4 (0.8%)	4862 (2047.5-6882.3)	
Chronic Diseases No.:			
0	76 (15.9%)	918 (243.8-1752..4)	
1	87 (18.2%)	1063 (449-2208)	
2	76 (15.9%)	1031 (466.5-2197.8)	0.200
3	85 (17.7%)	1572 (434-2337)	
≥4	155 (32.4%)	1167 (630-2508)	
DM Treatment:			
Insulin & OHDs	106 (22.1%)	1809 (772.3-2741)	
Healthy Lifestyle	50 (10.4%)	682.5 (189-1117)	0.000
Insulin	77 (16.1%)	945 (290.5-1953.5)	
OHDS	246 (51.4%)	1138 (492.8-2230)	

(Table 2) contd….

Variable	Frequency (%)	Health Care Cost Median (Interquartile Range)	*p*-Value
Insulin Duration:			
No Insulin	297 (62%)	1068 (454.5-2137)	0.265
1-7 years	108 (22.5%)	1362.5 (669.5-2413.5)	
8-14 years	40 (8.4%)	1327.5 (266.0-2725)	
15-23 years	19 (4%)	1032.5 (245-2560)	
≥ 24 years	15 (3.1%)	993 (237-2412)	
Medications No.			
≤3	267 (55.7%)	896 (360-1972)	0.000
4-6	146 (30.5%)	1267.5 (589.5-2605.8)	
≥7	66 (13.8%)	2088 (929-3599.3)	
Hospital Admission			
No	348 (72.7%)	1014 (449.3-2084)	0.000
Yes	131 (27.3%)	1873 (700-4057)	
Hospital type			
No Admission	350 (73.1%)	1014 (449.8-2088.3)	0.000
Governmental	92 (19.2%)	1850.5 (676.8-3168)	
Private	34 (7.1%)	1942.5 (712-5478.3)	
UNRWA	3 (0.6%)	1088 (348-556.5)	
Alternative Medicine			
No	276 (57.6%)	1055.3 (370.5-2218)	0.041
Yes	203 (42.4%)	1150 (594-2380)	
OTC			
No	276 (57.6%)	1081 (454-2260)	0.294
Yes	203 (42.4%)	1139 (706-2226.8)	

3.2. Diabetes Mellitus Costs

The estimated total health care cost incurred by participants and family members was Israeli Shekel (ILS) 988,276 (US Dollar 307,590) per year. Time loss costs accounted for the largest share (66.3%) of the total health care cost; about 17.1% was for direct nonmedical costs and 16.6% for direct medical costs. Medication costs accounted for 62.7% of total direct medical costs and 10.4% of the total health care cost, respectively. Moreover, lab test costs accounted for 37% of the total direct medical costs and only 6.1% of the total health care cost, respectively. The lowest total health care cost was found among the age group of 18-27 years (median (inter-quartile range: Q1-Q3) = 594.5 (215.8-1589.3)), while the age group of ≥ 58 years old acquired the highest total health care cost (median (inter-quartile range: Q1-Q3) = 1250 (631.3-2413.5)). Median (inter-quartile range: Q1-Q3) total health care cost for male participants was 1074 (450-2217), which was found to be lower than the same for female participants which was found to be 1123 (532.3-2298.8).

Furthermore, the highest total health care cost was found for those who stated that they were married and their household monthly income to be 2000-4999 ILS (median (inter-quartile range: Q1-Q3) = 1178.5 (567-2409), 1182 (472.5-2415), respectively). In addition, the highest total health care cost was incurred by participants whose educational level was middle and high school level and those village residents (median (inter-quartile range: Q1-Q3) = 1378 (666-2412) & 1142 (545-2416), respectively). Subsequently, the highest total health care cost was found among participants whose employment status was home duty (median (inter-quartile range: Q1-Q3) =1347 (666-2365)). However, significant differences in total health care costs ($p < 0.05$) were found only among participants with different age ($p < 0.005$), marital status ($p < 0.001$), educational level ($p < 0.001$), and residency place ($p < 0.05$) (Table **1**).

A total health care cost was found to be significantly highest among participants who received combination treatment of OHDs and insulin for DM management, and those who received 7 and/or more medications daily (median (inter-quartile range: Q1-Q3) = 1809 (772.3-2741), 2088 (929-3599.3), respectively, $p < 0.001$). Moreover, a significant difference in total health care costs was found among participants who were admitted to the hospital (median (inter-quartile range: Q1-Q3) = 1873 (700-4057), $p < 0.001$). Furthermore, total health care cost was significantly higher among participants who took herbal products and medicinal plants as an alternative medicine for DM management (median (inter-quartile range: Q1-Q3) = 1150 (594-2380), $p < 0.05$). In addition, the median (inter-quartile range: Q1-Q3) the total health care cost for participants who were admitted to Palestinian private hospitals was 1942.5 (712-5478.3),

Table 3. Multiple linear regressions of factors related to total health care cost.

Variable	Standardized Coefficient (Beta)	Unstandardized Coefficient (B)	SE	T	*p*-value
Age	-0.106	-330.8	181.3	-1.8	0.069
Marital Status	-0.037	-150.2	210.4	-0.714	0.476
Educational Level	-0.054	-335.1	317.01	-1.1	0.291
Residency Place	0.055	429.2	353.6	1.214	0.225
Diabetic Treatment	-0.063	-234.3	173.8	-1.3	0.178
Medications Number	0.090	569.8	327.2	1.7	0.082
Hospital Admission	0.136	1392.0	1077.0	1.292	0.197
Hospital Type	-0.038	-272.9	750.3	-0.364	0.716
Alternative Medicine	0.091	843.9	425.4	1.984	0.048

which was significantly ($p < 0.05$), the highest among participants who were admitted to other hospitals in Palestine (Table **2**). However, Table **3** shows that adjusting covariates using multiple linear regressions found that there was a significant association between only alternative medicine use and total health care cost ($p < 0.05$).

3.3. Factors Associated with Medication Adherence

More than half of the participants were adherent to prescribed medications (52.2%), while the others were non-adherents (47.8%). Tables **4** and **5** show that univariate analysis showed that there was a significant association between MA and DM duration ($p < 0.005$), hospital admission ($p < 0.005$), hospital type ($p < 0.05$), and alternative medicine use ($p < 0.05$). Participants whose educational level was school and university level were less likely to be adherent to prescribed medications ((OR=0.326; 95% C.I of 0.140-0.758) and (OR= 0.372; 95% C.I of 0.144-(0.956), respectively) (Table **4**).

Furthermore, participants who were diagnosed with DM for 8-14 years and those since 15-23 years, respectively, were less likely to be adherent to prescribed medications ((OR=0.449; 95% C.I of 0.259-0.779) and (OR=0.313; 95% C.I of 0.147-0.666), respectively). However, participants with 1 chronic disease other than DM and those who received herbal products and medicinal plants as alternative medicine were more likely to be adherent to prescribed medications ((OR=4.628; 95% C.I of 1.359-15.578) and (OR=1.688; 95% C.I of 1.087-2.620) respectively). Moreover, participants who were admitted to hospitals and those who were admitted specifically to Palestinian governmental hospitals were more likely to be adherent to prescribed medications ((OR=1.839; 95% C.I of 1.224-2.763) and (OR= 1.809; 95% C.I of 1.135-2.881), respectively) (Table **5**).

In addition, univariate analysis showed that there was no significant difference between participants who were adherent and those who were non-adherent to prescribed medications in total health care cost, direct medical and nonmedical costs, and time loss cost (Table **6**). Furthermore, multivariate analysis showed that being in school study level and diagnosed with DM (*i.e.*, DM duration) since 8-14 years, 15-23 years, and ≥ 24 years were significantly related to decreased odds of MA. Moreover, the use of alternative medicine was significantly related to increased odds of MA. Thus, participants who used alternative medicine were more likely to be adherent to prescribed medications (OR=1.699, 95% C.I of 1.154-2.501) (Table **7**).

4. DISCUSSION

World Health Organization has declared DM to be an epidemic due to its rising prevalence. It is a complex condition produced by oligo- and polygenic hereditary variables, as well as non-genetic factors resulting from an imbalance in energy intake and output, as well as other lifestyle factors. One of the important aspects is the relationship between obesity and DM which is considered very complex. Many factors that link these 2 epidemics have been thoroughly investigated in the past. Obesity plays a role in the aetiopathogenesis of Type II DM, the most common type of DM in the world, as well as the development of its diabetic complications [24, 25].

Obesity and overweight play a growing role in Type I DM, according to scientific research. Weight gain is often thought of as a side effect of insulin therapy, but it also has a significant pathophysiological impact at different stages of the disease [26, 27]. The highly variable microbiome is another significant feature of DM and obesity. The gut microflora's function, its interaction with the rest of the body, and its role in the development of obesity Type I DM, and Type I DM are all still unknown and subject of ongoing investigations [28, 29].

The complexity of this condition may reflect very high economic consequences as a multidimensional treatment could be necessary. Subsequently, the study results proved that there was a significant and clear discrepancy in total DM health care costs among participants who were admitted to hospital, which could be an inevitable result of decreasing MA rates and the resulting increase in the prevalence of poor glycemic control, that might lead to an increase in the incidence and prevalence of diabetic complications, that will result in the need for hospital admissions, and an increase in costs incurred by all community segments and health care providers [7].

Table 4. Univariate analysis of socio-demographic factors related to medication adherence.

Variable	Frequency (%) N=330	Adherent N=182 (55.2%)	Non-Adherent N=148 (44.8%)	Odds Ratio with 95% C.I	*p*–Value
Age category					
18-27	86 (18%)	46 (18.4%)	40 (17.5%)	Reference (1)	(0.271)
28-37	15 (3.1%)	8 (3.2%)	7 (3.1%)	0.576 (0.124–2.664)	0.480
38-47	41 (8.6%)	17 (6.8%)	24 (10.5%)	0.787 (0.171–3.623)	0.759
48-57	141 (29.4%)	69 (27.6%)	72 (31.4%)	0.551 (0.132–2.302)	0.414
≥58	196 (40.9%)	110 (44.0%)	86 (37.6%)	0.364 (0.088–1.506)	0.163
Gender					
Female	236 (49.3%)	130 (52%)	106 (46.3.3%)	Reference (1)	(0.636)
Male	243 (50.7%)	120(48%)	123 (53.7%)	1.175 (0.603–2.290)	0.636
Marital status					
Married	331 (69.1%)	172 (68.8%)	159 (69.4%)	Reference (1)	(0.866)
Separated/Divorced	4 (0.8%)	1 (0.4%)	3 (1.3%)	2.724 (0.218–34.06)	0.437
Single	91 (19%)	49 (19.6%)	42 (18.3%)	1.126 (0.338-3.755)	0.847
Widowed	53 (11.1%)	28 (11.2%)	25 (10.9%)	0.891 (0.394-2.018)	0.783
Income level (ILS)					
<2000	124 (25.9%)	62 (24.8%)	62 (27.1%)	Reference (1)	(0.509)
2000-4999	256 (53.4%)	138 (55.2%)	118 (51.5%)	0.898 (0.513-1.572)	0.705
5000-9999	78 (16.3%)	41 (16.4%)	37 (16.2%)	1.273 (0.599-2.705)	0.530
≥10000	21 (4.4%)	9 (3.6%)	12 (5.2%)	1.747 (0.544-5.613)	0.349
Educational level					
Literacy Study	48 (10%)	18 (7.2%)	30 (13.1%)	Reference (1)	(0.077)
Middle & High school	219 (45.7)	123 (49.2%)	96 (41.9%)	0.326 (0.140–0.758)	0.009
University Study	189 (39.5%)	95 (38%)	94 (41.0%)	0.372 (0.144–0.956)	0.040
Post Graduate Studies	23 (4.8%)	14 (5.6%)	9 (3.9%)	0.330 (0.087-1.253)	0.103
Occupation					
Home Duties	127 (26.5%)	72 (28.8%)	55 (24%)	Reference (1)	(0.951)
Own Businesses	80 (16.7%) 57 (11.9%)	38 (15.2%)	42 (18.3%)	1.317(0.537–3.228)	0.547
Private Sector Employee	51 (10.6%)	29 (11.6%)	28 (12.2%)	1.017 (0.386–2.682)	0.972
Public Sector Employee	38 (7.9%)	25 (10%)	26 (11.4%)	1.158 (0.441-3.042)	0.766
Retired	126 (26.3%)	22 (8.8%)	16 (7%)	0.852 (0.293-2.480)	0.769
Unemployed		64 (25.6%)	62 (27.1%)	1.131 (0.521-2.457)	0.755
Residency place					
Refugee camp	24 (5%)	14(5.6%)	10 (4.4%)	Reference (1)	(0.724)
City	172 (35.9%)	93 (37.2%)	79 (34.5%)	1.488 (0.507-4.366)	0.469
Village	283 (59.1%)	143 (57.2%)	140 (61.1%)	1.546 (0.534-4.474)	0.421

Table 5. Univariate analysis of clinical factors related to medication adherence.

Variable	Frequency (%) N=330	Adherent N=182 (55.2%)	Non-Adherent N=148 (44.8%)	Odds Ratio with 95% C.I	*p*–Value
Type of DM					
Type 1	142 (29.6%)	85(34%)	57 (24.9%)	Reference (1)	
Type 2	337 (70.4%)	165 (66%)	172 (75.1%)	1.410 (0.834–2.382)	0.199
Diabetes Duration					
1-7 years	228 (47.6%)	99 (39.6%)	129 (56.3%)	Reference (1)	(0.004)
8-14 years	126 (26.3)	73(29.2%)	53 (23.1%)	0.449 (0.259–0.779)	0.004
15-23 years	73 (15.2%)	47 (18.8%)	26 (11.4%)	0.313 (0.147-0.666)	0.003
≥ 24 years	52 (10.9%)	31 (12.4%)	21 (9.2%)	0.446 (0.193-1.028)	0.058
Smoking					
Yes	114 (23.8%)	53 (21.2%)	61 (26.6%)	1.381 (0.793-2.407)	0.254
No	365 (76.2%)	197 (78.8%)	168 (73.4%)	Reference (1)	
BMI:					
Underweight	10 (2.1%)	10 (4%)	0 (0%)	Reference (1)	(0.133)
Normal	125 (26.1%)	64 (25.6%)	61 (26.6%)	0.898 (0.513-1.572)	0.705
Overweight	186 (38.8%)	101 (40.4%)	85 (37.1%)	1.273 (0.599-2.705)	0.530
Obese	158 (33%)	75 (30%)	83 (36.2%)	1.747 (0.544-5.613)	0.349
Diabetic Compli-cations No.					
0	107 (22.3%)	59 (23.6%)	48 (21.0%)	Reference (1)	(0.323)
1	93 (19.4%)	49 (19.6%)	44 (19.2%)	0.336 (0.105–1.078)	0.067
2	84 (17.5%)	44(17.6%)	40 (17.5%)	0.320 (0.053–1.926)	0.213
≥3	195 (40.7%)	98 (39.2%)	97 (42.4%)	0.258 (0.023-2.908)	0.273
Non Diabetic Comorbidities No.:					
0	295 (61.6%)	156 (62.4%)	139 (60.7%)	Reference (1)	(0.318)
1	149 (31.1%)	81 (32.4%)	68 (29.7%)	0.526 (0.249-1.110)	0.092
2	31 (6.5%)	12 (4.8%)	19 (8.3%)	0.758 (0.201–2.858)	0.682
≥3	4 (0.8%)	1 (0.4%)	3 (1.3%)	0.427 (0.021-8.583)	0.578
Chronic Diseases No.:					
0	76 (15.9%)	47 (18.8%)	29 (12.7%)	Reference (1)	(0.125)
1	87 (18.2%)	40 (16%)	47 (20.5%)	4.628(1.359-15.758)	0.014
2	76 (15.9%)	43 (17.2%)	33 (14.4%)	4.135 (0.668-25.590)	0.127
3	85 (17.7%)	46 (18.4%)	39 (17%)	5.047 (0.442-57.627)	0.193
≤4	155 (32.4%)	74 (29.6%)	81 (35.4%)	8.388 (0.482-145.889)	0.144
DM Treatment:					
Insulin & OHDs	106 (22.1%)	55 (22%)	51(22.3%)	Reference	(0.538)
Healthy Lifestyle	50 (10.4%)	23 (9.2%)	27 (11.8%)	1.266 (0.645-2.484)	0.493
Insulin	77 (16.1%)	49(19.6%)	28 (12.2%)	0.616 (0.338-1.124)	0.114
OHDS	246 (51.4%)	123 (49.2%)	123 (53.7%)	1.078 (0.684-1.701)	0.754

(Table 5) contd….

Variable	Frequency (%) N=330	Adherent N=182 (55.2%)	Non-Adherent N=148 (44.8%)	Odds Ratio with 95% C.I	*p*-Value
Medications No. ≤3 4-6 ≥7	267 (55.7%) 146 (30.5%) 66 (13.8%)	148 (59.2%) 71 (28.4%) 31 (12.4%)	119 (52%) 75 (32.8%) 35 (15.3%)	Reference 1.314 (0.877-1.969) 1.404 (0.818-2.410)	(0.352) 0.186 0.218
Hospital Admission No Yes	348 (72.7%) 131 (27.3%)	196 (78.4%) 54 (21.6%)	152 (66.4%) 77 (33.6%)	Reference (1) 1.839 (1.224-2.763)	 0.003
Hospital type No Admission Governmental Private UNRWA	350 (73.1%) 92 (19.2%) 34(7.1%) 3 (0.6%)	196 (78.4%) 38 (15.2%) 14 (5.6%) 2 (0.8%)	154 (67.2%) 54 (23.6%) 20 (8.7%) 1 (0.4%)	Reference (1) 1.809 (1.135-2.881) 1.818 (0.890-3.716) 0.636 (0.057-7.083)	(0.042) 0.013 0.101 0.713
Alternative Medicine No Yes	276 (57.6%) 203 (42.4%)	158 (%63.2) 92 (%36.8)	118 (51.5%) 111 (48.5%)	Reference (1) 1.688 (1.087-2.620)	0.020
OTC Yes No	72 (15%) 407 (85%)	32 (12.8%) 218 (87.2)	40 (17.5%) 189 (82.5%)	Reference (1) 1.337 (.7442.402)	0.331

Table 6. Univariate analysis of costs related to medication adherence.

Cost	Cost Median (Interquartile Range)	Adherent	Non-Adherent	Odds Ratio with 95% C.I	*p*-value
Healthcare Cost	1104 (474-2259)	1065.5 (448.3-2212)	1142 (504.5-2413.5)	1.00 (1.00-1.00)	0.449
Direct Cost	227 (80-657)	268 (74.5-592)	297 (94-731)	1.00 (1.00-1.00)	0.470
Direct Medical Cost	212 (40-387)	183.5 (27.5-372)	222 (43-436)	1.00 (1.00-1.00)	0.147
Direct Non-Medical	60 (10-176)	60 (5-150)	52 (14-200)	1.00 (1.00-1.00)	0.819
Time loss Cost	676 (338-1690)	676 (232.4-1690)	760(338-1732.5)	1.00 (1.00-1.00)	0.493

Table 7. Multivariate analysis of factors related to medication adherence.

Variable	B	S.E	Wald	Odds Ratio with 95% C.I	*p*-Value
Diabetes Duration 1-7 years 8-14 years 15-23 years ≥ 24 years	-0.739 -1.081 -0.890	0.240 0.304 0.340	9.516 12.664 6.873	Reference (1) 0.478 (0.299–0.764) 0.339 (0.187-0.615) 0.411 (0.211-0.799)	(0.000) 0.002 0.000 0.009
Educational Level Literacy Study Middle & High school University Study Post Graduate Studies	 -0.888 -0.511 -0.811	 0.355 0.357 0.570	 6.264 2.044 2.023	 Reference (1) 0.411 (0.205-0.825) 0.600 (0.298-1.209) 0.444 (0.145-1.359)	 (0.056) 0.012 0.153 0.155

(Table 7) contd….

Variable	B	S.E	Wald	Odds Ratio with 95% C.I	*p*-Value
Chronic Diseases No.					
0	0.597	0.335	3.183	Reference (1)	(0.056)
1	0.101	0.349	0.083	0.411 (0.205-0.825)	0.012
2	0.226	0.342	0.437	0.600 (0.298–1.209)	0.153
3	0.422	0.313	1.827	0.444 (0.145-1.359)	0.155
≤4					
Hospital Admission					
No	21.274	27665.438	0.000	Reference (1)	0.999
Yes				1734427081 (0)	
Alternative Medicine					
No	0.538	0.201	7.182	Reference (1)	0.007
Yes				1.713 (1.156-2.539)	
Hospital Type					
No Admission				Reference (1)	(0.669)
Governmental	-20.504	27665.438	0.000	(0.000)	0.999
Private	-20.545	27665.438	0.000	(0.000)	0.999
UNRWA	-22.223	27665.438	0.000	0.00 (0.000)	0.999

Furthermore, clear and significant differences in total health care costs incurred by participants and their family members were also observed between admissions to private and public hospitals. This, in turn, is mainly due to decreased MA rates, followed by poor glycemic control and the resulting diabetic complications, as well as hospital admission and varying costs for both patients and health care providers, based on health insurance systems and the availability of health insurance for DM patients [30]. Subsequently, the significant increase in total DM health care cost according to hospital admissions and hospital type is an inevitable result of patient medication non-adherence, poor glycemic control, development of diabetic complications, and high probability of having non-diabetic comorbidities, which are poor health outcomes of DM health care.

Evaluation of the quality of DM health care is based on 3 main health outcomes represented by DSCMBs, glycemic control (*e.g*., HbA1c), and costs. Furthermore, DSCMBs dimensions include diet, physical exercise, testing, blood glucose levels, and MA, which is forming the basis for the assessment of all other DSCMBs dimensions [31]. Accordingly, the study results proved the importance of taking significant associations between alternative medicine, total DM, health care cost, and MA into consideration, which represents the condition of DM patients in Palestine and their community culture that deserves attention and research [32].

Poor glycemic control, development of diabetic complications, resulting admission to private and/or public hospitals, and increased DM costs incurred by patients and/or family members are related to poor health outcomes of DM health care that might have led to the use of medicinal plants as an alternative medicine for DM management without consulting doctors, and this, in turn, exacerbates the already aggravated problem and increased costs incurred by them [33]. Consequently, this increases the possibility that the Palestinian society believes that alternative medicine can be a good and safe alternative for DM patients to achieve desired health outcomes.

Several reasons can be an explanation for the results concerning alternatives; the most prominent is published research which enhanced the role of social media (*e.g*. Facebook) that may promote the use of herbs such as cinnamon for the management and treatment of DM in the absence of medical strategies concerning alternative medicine. However, the use of herbal products as alternative medicine can increase the economic burden on patients and society due to the additional costs that they incur in addition to the basic costs of DM management (*i.e*. direct costs and time loss costs) [34].

Moreover, DM in general and type 2 DM, in particular, is caused by both genetic and environmental factors. Scientists have linked several gene mutations to higher DM risk. Not everyone who carries a mutation will get DM. However, many people with DM do have one or more of these mutations. Therefore, the use of alternative medicine should be limited to a scientific and medical basis, as well as a clear strategy for ensuring their safety under the supervision and instruction of health care professionals (*e.g*. doctors) to obtain the best health outcomes and to save costs for patients, health care providers, and society.

It was noted through the study results that there is an inverse proportion between MA on the one hand, and the longer DM duration and use of medicinal plants as an alternative medicine on the other hand. Furthermore, the study results proved no significant relationships between DM costs and MA. Therefore, it is noticeable that there was a logical and sequential explanation for these results represented by lim-

ited awareness of the importance of DM health care among study participants according to their educational level and the risk of diabetic complications as a result of medication non-adherence, despite the passage of time since diagnosed with DM [35].

However, this is the best evidence of the lack of sufficient awareness among DM patients concerning the importance of adhering to medical instructions from health care professionals, and resorting to the use of medicinal plants as an alternative medicine without a clear medical strategy as a means of survival and way of hope to confront the bitter reality of poor glycemic control, increased diabetic complications, and DM costs, a health problem that is rooted in MA and DSCMBs. Thus, reinforces the need to strengthen the patient-health care professionals' relationship, and to enhance the role of preventive education in raising patients' awareness concerning the importance of great awareness about MA and DSCMBs, as well as the use of alternative medicine within a clear and evidence-based strategy to increase MA and patient compliance rates, improve glycemic control, prevent and/or avoid diabetic complications, and reduce costs.

CONCLUSION

It is concluded from this study there is a need to strengthen the patient-health care professional's relationship and to enhance the role of preventive education, the importance of awareness about MA, DSCMBs, and the use of alternative medicine based on evidence-based strategies to improve MA, glycemic control, meanwhile reducing the costs incurred by patients and family members.

LIST OF ABBREVIATIONS

BMI	=	Body Mass Index
DM	=	Diabetes Mellitus
DSCMBs	=	Diabetes Self-Care Management Behaviors
IRB	=	Institutional Review Board
MA	=	Medication Adherence
OHDs	=	Oral Hypoglycemic Drugs

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Institutional Review Board (IRB) of An-Najah National University in Nablus (West Bank of Palestine) with a reference number of Phr/05/2015.

HUMAN AND ANIMAL RIGHTS

The study was performed in compliance with the Helsinki Declaration for research in humans.

CONSENT FOR PUBLICATION

All participants provided their informed consent to participate in this study before they were included.

STANDARDS OF REPORTING

STROBE guidelines were followed in this study.

AVAILABILITY OF DATA AND MATERIALS

The dataset that support the results and finding of this research are available from the corresponding author [RM], upon reasonable request.

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None.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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