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Article

Medication-related burden among patients with chronic disease conditions: perspectives of patients attending non-communicable disease clinics in a primary healthcare setting in Qatar

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Abstract: The aim of this cross-sectional study was to assess the perceived medication-related burden among patients with multiple non-communicable diseases (NCDs), and to investigate the association between perceived burden and adherence to medication therapy. Medication-related burden was measured in three primary care clinics in Qatar using the Living with Medicines Questionnaire (LMQ) among adults with diabetes, with or without other comorbidities. Adherence was measured using the Adherence to Refills and Medications Scale (ARMS). Two hundred ninety-three eligible patients participated in the study. Majority of participants reported experiencing minimum (66.6%) to moderate (24.1%) medication-related burden. There was a significant positive correlation between the medication-related burden (measured by the LWQ) and medication adherence (measured by ARMS) (r_s (253) = 0.317, $p < 0.0005$). The duration of diabetes diagnosis, adherence score, marital status, employment status, and presence diagnosis of hypertension were significant predictors of medication burden. A considerable proportion of the patients in this study have reported experiencing medication-related burden. Healthcare providers should seek strategies to address this burden especially among patients with risk factors of cardiovascular diseases, non-adherent to their medication therapy, living alone, or non-employed.

Keywords: Medication-related burden, Questionnaire, chronic disease conditions, adherence.

1. Introduction

Non-communicable diseases (NCDs) are associated with increasing prevalence of morbidity and mortality globally [1]. Despite concerted global efforts aimed at reducing the burden of these diseases [2-4], the main focus of healthcare systems and clinical practice guidelines in general is to achieve and maintain clinical therapeutic goals for single conditions when managing chronic illnesses [5-7]. This type of fragmented care approach would lead to diminished quality of life among people with multimorbidities [7].

Medications are commonly used for the long-term management of chronic diseases [8]. The benefits of medications in preventing or slowing the progression of the adverse consequences of NCDs including premature deaths, as well as managing associated symptoms, are indisputable [8]. Polypharmacy, defined as the use of multiple medications [9], could be perceived as an unavoidable consequence of the advancement in the treatment strategies of today's aging population [9-11]. Paradoxically, polypharmacy has also been associated with increased morbidity and mortality, hospitalizations, and demand for nursing home care [12, 13].

The traditional focus of clinical practice guidelines on individual diseases, the increasing coexistence of multiple comorbid conditions, and the lack of structured strategies to manage problems associated with the consequences of treatments meant that patients with multiple NCDs have to deal with extremely complex instructions and tasks associated with medications for the rest of their lives [14]. Coping with adverse consequences of medications and having to tailor life activities according to the demands of therapeutic regimens result in putting an extra burden on patients [6, 15, 16]. Thus, the experience of using medications and health care, especially for long durations, as a potentially critical threat to success of treatment regimens, is worth investigating [17, 18].

The concept of "medication-related burden" has been well-described in the literature [15, 17, 19-21]. Studies have also highlighted the association between this burden and adherence to medication therapy [6, 15, 21, 22]. Although the concept of treatment burden is increasingly attracting attention from various research groups, studies that mainly focused on the association between the treatment burden and adherence to therapy are scarce, mainly used qualitative methodology, and focused on specific diseases [23, 24].

The Qatar's National Health Strategy, and its updates declared the establishment of a world-class healthcare system aiming to provide a comprehensive primary care model that puts the patient at the center of care [25-27]. Through NCD clinics established in primary health centers that provide care for all patients with chronic diseases in Qatar, Primary Health Care Corporation (PHCC) guarantees primary care services emulating the recommended transition in health care globally, as well as the plans and strategies that are aimed at reducing the mortality and burden related to the NCDs. [25,26]

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Assessment of the medication-related burden, from the patient's perspective, is an important endeavor to appraise National Health Strategies of any barriers that may hinder the optimum use of health services at the primary health care level. Moreover, previous studies have qualitatively reported the association between perceived medication-related burden and the patients' well-being as well as adherence to therapy. To our knowledge, this association has not yet been quantitatively measured among patients with NCDs. This study aimed to assess the burden resulting from the treatment of chronic NCD conditions in Qatar and its impact on medication adherence.

2. Materials and Methods

This cross-sectional study was conducted among patients with chronic NCDs in Qatar to measure perceived medication-related burden and its association with medication adherence. Ethical approval to conduct the study was obtained from the Research Section (Clinical Affairs) of the PHCC (approval no. RC Ref. PHCC/RC/15/10/015).

Primary health care services are provided by the PHCC, to patients with NCD living in Qatar, through 23 health centers that host NCD clinics [26, 27]. For this study, three centers providing such services were selected. The selection of the clinics was based on the ethical approval conditions, the approximate similarity in demographic distribution of patients' visits across the health centers, and based on the fact that all the three centers have NCD clinics [26].

Although the perceived medication-related burden is expected to be associated with seeking treatment for any chronic illness [21], patients in this study were recruited if they had diabetes mellitus (DM), with or without comorbidities (other NCDs). DM is considered an excellent representative of NCDs that sit on the top of Qatar's health strategy due to their high prevalence and impact of people's lives [26]. Patients were eligible for enrollment in this study if they were at least 18 years of age, diagnosed with diabetes for at least 6 months prior to the study (with or without other comorbidities), and able to communicate in English and/or Arabic. As 13.5% of the population in Qatar has diabetes [28], and the medication-related burden was assumed to exist with all of them, the sample size was estimated using the following equation [29]:

$$\text{Sample size} \quad = \quad \frac{(Z_{1-a/2})2\ P\ (1 - P)}{d2}$$

Where $Z_{1-a/2}$ is standard normal variate, which is 1.96 at 5% level of confidence; P is the expected proportion in the population (P=0.135); and assuming an absolute error (d) to be 0.05.This number was increased by 30% to account for missing data. Hence, a total of 234 patients was the target for this study.

The primary outcome measure was the self-reported medication-related burden (including LMQ score and the VAS score). Self-reported adherence was assessed as a secondary outcome measure.

2.1. Data collection measures

Below is a description of the two instruments used in the study:

1. **The Living with Medicines Questionnaire** (LMQ) [30, 31]: This is a 41-item questionnaire with which respondents are required to indicate their level of agreement using a five-point Likert-type scale (from strongly agree to strongly disagree). In addition, a free text (open-ended) question

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accords the respondent the opportunity to add any other relevant issues that are not covered in the questionnaire. The tool comprised of eight domains: Relationships with health professionals, Practicalities, Information, Efficacy, Side effects, Attitudes, Impact, and Control. The overall LMQ score was the sum of the scores of all the 41 items in the questionnaire, and ranged from 41 to 205, with higher scores indicating higher burden. The questionnaire also contained a VAS, through which respondents provided a global assessment of the overall burden they experience (0 to 10 points, with higher scores representing higher perceived burden). This tool was validated in English [30] and translated into the Arabic context using best practices [31]. Both the Arabic and the English versions were used in this research, as applicable.

2. The Adherence to Refills and Medication Scale (ARMS) [32]: This is a 12- item questionnaire that had also been validated in English, and translated into the Arabic context by the research team in coordination with the original developers of the tool. The ARMS score was the sum of the scores of the 12 items in the scale, and ranged from 12 to 48, with higher scores indicating worse adherence. The ARMS was developed to measure adherence to drug therapy and was validated among patients prescribed long-term therapy for coronary heart diseases [32]. The scale demonstrated a high internal consistency reliability (Cronbach's α=0.814) and a significant correlation with Morisky Adherence Scale (Spearman's rho =-0.651, $P < 0.01$) [32]. Both the Arabic and the English versions were used in this research, as appropriate.

2.2. Data analysis

Descriptions and comparisons using frequencies and percentages were used to describe all the variables in the study, and to express the perceived medication-related burden among the participants. Inferential statistics (univariate analysis) were also used to determine and compare the medication-related burden scores across different demographic and clinical characteristics. In order to demonstrate the relationship between the perceived medication-related burden and adherence to medication therapy, correlation analysis was applied [33]. As reported in the literature, perceived medication-related burden was assumed to be associated with medication adherence [21, 22]. Given the cyclic nature of perceived burden [21], the direction of this association was not hypothesized in this study. In order to further explain the score of the medication burden after accounting for the measured variables altogether, regression analysis was used.

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3. Results

Of the 500 eligible patients approached, 307 consented to participate in the study. After excluding forms with incomplete, or invalid data (i.e. the participant responded to only one questionnaire, or responded with neutral response to all the items of the LMQ), a total of 293 participants were included in the analysis (still exceeding the estimated sample size required). Around 86% of the participants provided complete responses to all of the items in the LMQ.

Tables 1 and 2 contain the sociodemographic, clinical, and other characteristics of the study sample. Most of the participants were young to middle age adults (78.4%), male (71%), non-Qataris (non-Qatari Arabs 41.6%), married (94.9%), educated (54.3% with university degree or higher), and employed (70.4%). The majority of the participants (66.6%) reported that they were not following any lifestyle changes recommended by their healthcare providers. Smoking history (cigarette and/or shisha) revealed that the majority of the studied cohort was never smoker.

The median (IQR) duration of DM diagnosis was 8.0 (8.0) years, with the majority (66.6%) diagnosed from 6 months to 10 years ago. Most of the participants (90.1%) had comorbidities, with 77.1% having up to three comorbidities. The most commonly reported comorbidities were; hypertension (55.3%), dyslipidemia (55.3%), and obesity (48.1%). Participants were prescribed with a median (IQR) of 5.0 (3.0) medications, and 6.0 (3.0) daily doses. In addition, approximately 29% of the participants were prescribed more than five medications. The diabetes control status of the patients was determined using the most recently available HbA1c value in the medical records. The median (IQR) HbA1c value was 7.80% (2.3), and 66.2% of the participants had uncontrolled DM (HbA1c greater than 7%). In addition, the median (IQR) Body Mass Index (BMI) of the study participants was 29.98 (6.68) kg/m^2.

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Table 1. Sociodemographic characteristics of the participants (N = 293)

Variable	Frequency (%)
Age (years)	
Up to 65	256 (87.4)
Above 65	37 (12.6)
Gender	
Male	208 (71.0)
Female	85 (29.0)
Country of origin/ ethnicity	
Qatar	41 (14.0)
Arab countries (excluding Qatar)*	122 (41.6)
Indian subcontinent**	107 (36.5)
Philippines	14 (4.8)
Others***	9 (3.1)
Education Level	
Less than primary school	3 (1.0)
Primary or middle school	47 (16.0)
Secondary school	52 (17.7)
Technical college	32 (10.9)
University degree	145 (49.5)
Postgraduate degree	14 (4.8)
Marital status	
Married	278 (94.9)
Single	7 (2.4)
Divorcee	5 (1.7)
Widowed	3 (1.0)
Lifestyle changes	
None	184 (62.8)
Exercise	103 (35.2)
Exercise & healthy diet	6 (2)
Cigarette smoking	
Current smoker	32 (10.9)
Former smoker	42 (14.3)
Never smoker	219 (74.7)
Shisha smoking	
Current daily smoker	8 (2.7)
Current social smoker	11 (3.8)
Former smoker	16 (5.5)
Never smoker	258 (88.1)
Employment	
Employed	205 (70.4)****
Unemployed	68 (23.4) ****
Retired	17 (5.8) ****
Full-time student	1 (0.3) ****

*Arabs countries include: Egypt, Jordan, Lebanon, Palestine, Sudan, Syria, Yemen, Iraq, Tunisia, and Morocco.

**Indian subcontinent include: India, Pakistan, Sri Lanka, and Bangladesh.

***Others include: Eretria, Hungary, Iran, Germany, Canada, Kenya, Brazil, and Britain

****Percentages total may not be 100% due to some missing responses.

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Table 2. Clinical Characteristics of the Study Participants (N = 293)

Variable	Median (IQR)	Frequency (%)
Duration of DM diagnosis	8.0 (8.0)	
6 months to 10 years		167 (66.5)*
More than 10 years		84 (33.5) *
Presence of co-morbidities		264 (90.1)
Number of co-morbidities		
One		93 (31.7)
Two		104 (35.5)
Three or more		67 (22.9)
Hypertension		162 (55.3)
Dyslipidemia		162 (55.3)
Vitamin D deficiency		18 (6.1)
Thyroid dysfunction		10 (3.4)
Obesity		141 (48.1)
Asthma		6 (2)
Others*		19 (6.5)
Number of prescribed medications	5.0 (3.0)	
Up to 5 medications daily		208 (71)
More than 5 medications daily		85 (29)
Medication type		
Tablet/ capsules		211 (72)
Any other type		82 (28)
Help with medicines		88 (30.4)*
HbA1c	7.80% (2.3)	
DM control status		
Controlled**		85 (29)*
Uncontrolled		194 (66.2)*
BMI*** (Kg/m^2)	29.98 (6.68)	

*Percentages total may not be 100% due to some missing responses.
**(HbA1c ≤ 7%)
***Body Mass Index

Perceived medication-related burden was measured among the participants using the LMQ. The median (IQR) LMQ score and VAS score were 95.00 [22] (possible range: 41 to 205) and 3.00 (4) (possible range: 0 to 10), respectively. The findings showed that the majority of the participants experienced from minimum (66.6%) to moderate (24.1%) degrees of burden (Table 3)

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Table 3. Perceived Medication-Related Burden Measured Using LMQ in Patients Attending NCD Clinics in Qatar (N = 293)

Variable	Range	Mean (SD)	Median (IQR)	Frequency (%)
LMQ overall score*	(41–205)	97.5 (18.6)	95.0 (22)	
No burden at all	(41–73)			18 (7.1)
Minimum burden	(74 –106)			169 (66.8)
Moderate degree of burden	(107–139)			61 (24.1)
High burden	(140–172)			5 (2)
Extremely high burden	(173–205)			-
Theme 1: Relationships with healthcare professionals about medicines	(5–25)	9.74 (3.12)	9.0 (4.0)	
Theme 2: Practical difficulties	(7–35)	15.19 (4.0)	15 (5.0)	
Theme 3: Cost-related burden	(3–15)	6.75 (2.80)	6.0 (4.0)	
Theme 4: Side effects of prescribed medications	(4 – 20)	9.65 (3.72)	8.0 (5.0)	
Theme 5: Effectiveness of medicines	(6 – 30)	11.36 (2.9)	12.0 (3.0)	
Theme 6: Attitudes/concerns about medicines use	(7 – 35)	20.35 (5.3)	20.0 (9.0)	
Theme 7: Impact/Interference to day to-day life	(6 – 30)	14.31 (4.4)	13.0 (6.0)	
Theme 8: Control/ Autonomy to vary regimen	(3 – 15)	10.17 (2.6)	10.0 (4.0)	
VAS: global burden	(0 – 10)	3.17 (2.5)	3.0 (4)	

*Total of LMQ with complete responses is 253 due to some missing responses

Furthermore, only 14 participants responded to the open-ended question regarding their views about how medication-related burden affected their lives. Ten issues emerged from their comments. These issues are summarized in Table 4.

Table 4. Additional Issues Contributing to Medication Burden Identified by the Study Participants (N=14)

No.	Issues identified in the comment
1	Travel time to utilize healthcare
2	Side effects of the medicines
3	Technical issues of medicines' refill system
4	Long waiting periods before seeing the physician
5	Seeing different physician for each follow-up appointment
6	Lack of information and instructions to live with their health conditions
7	Worry about taking several medicines at the same time, and about side effects of medicines
8	Worry about the long-term effects of the chronic condition on the body organs
9	Lack of information regarding the side-effects of the medicines, and their effect on the body
10	Feeling that follow-up appointments are not enough

Adherence was measured using ARMS, and the results showed that 84% of the participants were non-adherent to their prescribed medications (Table 5).

Table 5. Self-Reported Adherence of Patients with Chronic Conditions Attending NCD Clinics in Qatar Measured By ARMS (N = 293)

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Variable	Mean (SD)	Median (IQR)	Frequency (%)
ARMS overall score	17.4 (4.8)	16.0 (7)	
Adherent			47 (16)
Non-adherent			246 (84)

Mann-Whitney *U* and Kruskal-Wallis tests were used to determine the influence of sociodemographic and clinical characteristics of participants on perceived medication burden. Median LMQ score for Qatari was significantly higher, representing worse medication-related burden, than that for non-Qatari, ($p = 0.011$). Participants who had spouses showed significantly lower LMQ scores than participants who did not ($p = 0.002$). There were statistically significant differences in median LMQ scores between employed and non-employed participants, ($p = 0.044$). Furthermore, participants diagnosed with DM for more than 10 years showed statistically significantly higher median LMQ score than that of participants who had the diagnosis for less than 10 years ($p = 0.007$).

According to VAS scores representing global burden, participants with uncontrolled DM reported significantly higher global burden than participants with controlled DM ($p = 0.018$). The median VAS score for participants diagnosed with DM for more than 10 years was significantly higher than that for participants diagnosed with DM for less than 10 years ($p = 0.043$).

A Spearman's rank-order correlation test was used to assess the relationship between perceived medication-related burden and adherence to prescribed medications among the study population. There was a moderate positive correlation between LMQ score and ARMS score, $r_s(251) = 0.317$, $p < 0.0005$.This correlation implies that the higher is the medication-related burden, the lower is the medication adherence level (Given that the higher ARMS score translates into lower adherence, and higher LMQ score translates into higher burden). There was also a moderate positive correlation between the VAS scores and the ARMS score, $r_s(284) = 0.325$, $p < 0.0005$. This indicates also that the more perceived the medication burden is, the lower is the level of medication adherence.

To further understand the effect of the ARMS score (adherence) on the LMQ score (medication-related burden), a simple linear regression was performed. The prediction equation was: LMQ score = 74. 509 + 1.317*ARMS score. Average ARMS score significantly predicted LMQ score, $F(1, 249) = 35.85$, $p < .0005$, accounting for 12.6% of the variation in burden score with adjusted $R^2=0.122$, a medium effect size according to Cohen (1988). An extra one score of ARMS representing non-adherence leads to 1.317 increase in medication burden (95% CI, 0.884 to 1.751).

A stepwise multiple linear regression was conducted to determine if the addition of the other collected variables improve the explained variance and prediction of the LMQ score. The multiple regression model significantly predicted LMQ score, $F(5, 204) = 13.212$, $p < .0005$, adj. $R^2 = 0.226$. The variables that added statistically significant changes to the prediction were ARMS score, DM diagnosis duration, marital status, employment status, and presence of hypertension (HTN). Regression coefficients and standard errors can be found in Table 6.

Table 6. Coefficients and Standard Errors of Multiple Regression Analysis Predicting Medication Burden Score

Variable	B*	SEB**	Beta ***
Intercept	98.113	4.361	
ARMS score	1.297	0.232	0.342****
Employment	-7.526	2.452	-0.191****
DM diagnosis duration	7.697	2.410	0.203****
Marital status	-13.578	5.180	0.161****
Hypertension	-4.768	2.290	-0.131****

* B = unstandardized regression coefficient

**SEB = standard error

*** Beta = Standardized coefficient

****P < 0.05

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4. Discussion

This study was the first to measure medication-related burden from the perspective of patients living with chronic diseases, attending NCD clinics at PHCC in Qatar. As the majority of the patients visiting NCD were suffering from diabetes, we deliberately investigated medication-related burden among patients with diabetes as the main NCD disease focus. The LMQ was used to measure aspects of medication-related burden experienced by the NCD patients. Although almost all of the participants interviewed found this measure extremely relevant, the majority of them commented on the length of it. This might explain why only a minority of participants provided comments in the open-ended question at the end of the questionnaire. Our cohort of patients resembled the population in Qatar [34], with the majority of them being males, and from different nationalities. As expected, and similar to previous studies [35, 36, 37], most of our participants suffered several comorbidities, had been prescribed several medications, were non-adherent to their therapy, with uncontrolled diabetes, and adopted a sedentary lifestyles.

As the interest in conceptualizing and measuring medication-related burden is relatively new, there are currently only few studies to compare our results to. Out study is one of the first studies to assess medication-related burden among patients with NCDs from the perspective of the patients as an independent measure from the disease or medication context [36]. Our study indicated that a considerable proportion of the participants (90%) were suffering from varying degrees of burden related to their medication and overall treatment. As expected, this burden was minimal to moderate, given the high quality services provided to NCD patients in Qatar at minimal cost, and in one clinical setting. The results of the current study can best be compared to the results of a recent study conducted in Australia, which assessed overall treatment burden among patients with chronic conditions [36]. Although in that study, Sav. et al used a different tool (The Treatment Burden Questionnaire; TBQ), the main focus of their measurement was almost identical to that of the current study. They have also found that, independently from the ailment itself, treatment burden affected considerable proportion of patients with chronic diseases. Similar to our study, they have further highlighted the effects of patients' characteristics on the perceived burden [36].

Additionally, participants of Qatari nationality, female gender, unmarried, unemployed, diagnosed with DM for more than 10 years, having uncontrolled DM, and being prescribed with medication types other than tablets or capsules demonstrated significantly higher scores of medication burden. Cultural differences between Qatari nationals and non-Qatari residents could translate into different levels of perceiving burden resulting from medication therapy. As indicated in other studies, females tended to show higher levels of burden than males [20, 38]. These findings also indicate that having someone to provide support, and having a job could reduce the burden perceived by the patient. Our results also highlight the impact of the controlled status of the chronic condition on living with less burden. As expected, living longer with the disease, or being prescribed with any other dosage form other than pills, could translate into more discomfort with the treatment and its consequences.

As pointed out, only few participants (n = 14) responded to the open-ended question that asked respondents to raise any issues related to medication intake. These respondents raised 10 burdensome issues. Among them, only five were not covered in the LMQ. The newly emerging issues include travel time to utilize treatment, waiting time, issues related to the refill system, having to meet different physician in each appointment, and lack of sufficient number of follow-up appointments. Those highlighted burdensome issues were discussed in other studies focusing on overall treatment burden [20, 21, 38].

This study also found significant positive association between the scores of medication burden and self-reported medication adherence, which further supports previous qualitative studies suggesting lack of adherence among patients who experience medication burden [11, 20]. In a study that used the TBQ among patients with chronic conditions from many English-speaking countries, Tran et al. found higher perceived burden among patients with lower levels of adherence [16].

As adherence alone explained only 12% of medication-related burden, we further incorporated all the possible confounding factors in a regression model in an attempt to investigate the factors that can explain or predict the perceived medication-related burden. Regression results suggest that the mean medication burden for participants diagnosed with diabetes for less than 10 years, without spouse, and not employed, will be 98.113 (minimum burden) (standard error 4.361), out of possible score 205. The presence of hypertension surprisingly reduces the burden score by -4.768 (standard error 2.290). This finding contradicts the finding by Sav. et al who highlighted that having extra chronic condition would lead to increase treatment burden [36]. Furthermore, the presence of spouse as well as having a job were associated with reduced medication burden score by 7.526, 13.578, respectively. This is expected, since the evidence from the literature suggests that having familial support in the life of the patients with chronic disease [36], as well as a steady job reduces the perceived burden. Finally, exceeding 10 years of living with the chronic condition (diabetes in our case) increased burden score by 7.697 (standard error 2.410). Although one would assume that living more with the disease could mean learning more about it, getting used to its management, and hence feeling less burden, our results suggest that this was not the case in our sample. This could be explained by the possibility that the longer someone suffers a health condition and uses treatment for it, the more he/she experiences multiple issues related to long-term adverse treatment effects.

This study has several limitations that warrant mentioning to benefit future research. First, since it was a cross-sectional study, it implies that we were unable to capture all factors that might have affected medication-related burden over time. Longitudinal studies would be better capable to

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investigate the effect of those factors on perceived burden over time. Second, while self-reported adherence is still considered the most feasible, user-friendly, and simple means to measure medication adherence [39], combination of subjective and objective methods of measuring adherence is recommended [40]. Third, this study was limited to patients who were able to communicate in English or Arabic. Hence, the results cannot be generalized to people coming from different cultures, constituting a considerable proportion of the population in Qatar. In fact, perceived burden could be affected by factors related to the differences in beliefs about medications [21]; and such differences can also be related to culture. Future studies investigating these factors are recommended. Fourth, although our sample demographic information resembles those of the population in Qatar, it may not be representative of it due to the limitation of sampling technique. Finally, we have attempted to investigate the effect of confounding factors on the perceived medication burden. The results of this investigation could be considered preliminary, as the main focus of the study was not about investigating this effect, and the sample size was not calculated based on regression analysis. Future studies (qualitative and quantitative) focusing on highlighting the predictors of medication-related burden are needed.

5. Conclusions

A considerable proportion of patients experienced medication-related burden, which could be affected by many factors including adherence to drug therapy, duration of chronic disease diagnosis, control of the disease, being employed, or receiving support from family. Our study findings suggest that healthcare professionals should be aware of the impact of treatment plans on the lives of patients with chronic diseases. In addition, factors affecting medication-related burden should be taken into consideration when designing tailored interventions to reduce this burden.

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