



Medication-related burden from the perspective of the elderly

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Abstract

Background and aims. Extensive polypharmacy in the elderly population affects their quality of life and medication compliance. The UK-developed LMQ-3 (Living with Medicine Questionnaire-3) is a valid instrument designed to quantify medicine burden.

The aims of this study were to assess the medication-related burden among Bahraini elderly population in relation to their medication consumption patterns and other socio-demographic characteristics and identify specific issues that need to be addressed from the responses.

Methods. The descriptive cross-sectional study was designed to interview 500 Bahrainis over 65 years of age, by using an LMQ-3 questionnaire. Sample size was determined by Slovin's formula. Data on socio-demographic characteristics and medication consumption patterns were collected, then LMQ-3 and domain scores were compared by patient characteristics using descriptive statistics and statistical tests.

Results. We found a wide range of burden among participants in Bahrain, ranging from moderate burden in almost a third of participants, to high burden, over two-thirds of participants. Burden was mainly driven by concerns about medicines, interferences of medicines with daily life and side effects. Higher LMQ-3 scores were associated with those who were technical colleges graduates (7.5, $p < 0.001$), aged ≥ 75 years (7.7, $p < 0.001$), using ≥ 9 medicines (7.4, $p < 0.001$), or using medicines four times a day (7.5, $p < 0.001$). Anti-diabetics were the most prescribed medicines for the elderly.

In conclusion, high medication related burden was observed in the majority of patients with the highest seen in certain categories of participants such as the employed and the technical college graduates. Patients with the highest medication related burden should become the main target for practitioners and pharmacists.

Keywords: polypharmacy, compliance, elderly, burden, adherence, LMQ-3, medication awareness, communication

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Introduction

A high rate of polypharmacy is an inevitable result of the increasing rate of multi-morbidity in the elderly population worldwide, affecting almost one million older patients, and the number is increasing as the population ages [1]. The WHO (World Health Organization) has predicted that the number of older people defined as ≥ 65 years worldwide will reach 1.5 billion by 2050 [2]. This population growth carries significant challenges for health-care systems, as older patients use a significant amount of healthcare resources, which are mostly medications [3]. There are different definitions for polypharmacy including quantitative measures such as the use of multiple medications daily by a patient or consumption of more medicines than clinically indicated [4,5]. There are also qualitative measures, including the inappropriate use of medication or unnecessary medicines involving therapeutic duplication, as well as associated terms such as minor, moderate and major polypharmacy [5]. Although there is no universally accepted definition of polypharmacy, it can be described as being appropriate [1]. According to the WHO, appropriate polypharmacy occurs when all medications meet the specific therapeutic objectives with reduction in adverse drug reactions [2]. Most studies reported that the use of five or more medications indicates polypharmacy [1].

On the other hand, inappropriate polypharmacy happens when one or more of the medications are not needed because of the absence of the indication, failure to achieve the therapeutic objectives, and exposing the patients to potential harm and adverse drug reactions [2]. Living with potentially inappropriate medication among the elderly affects their quality of life and medication compliance [2].

Generally, elderly patients are more likely to be exposed to polypharmacy compared to general population because of age, drug clearance decreases and might as well lead to an increase in the risk of adverse drug reactions and negative health outcomes which have a significant impact on mortality and the likelihood of being hospitalized [6]. Moreover, the elderly patients' safety on multiple medications is not certain as the pre-market approval of any new medication usually requires the investigation of the effectiveness and safety which is traditionally achieved through different phases of randomized controlled trials, where elderly patients with multiple chronic conditions are usually excluded [7]. Therefore, our understanding of the negative consequences of polypharmacy in an older, multi-morbid population is limited [7]. The absence of clinical safety and the lack of studies on effectiveness in the elderly highlights the importance of pragmatic clinical trials which are conducted to include the patients of multi-morbidity and polypharmacy [8]. A pragmatic approach is needed, as it can be extracted from real world health-care data to focus

on patients at particularly higher-risk of polypharmacy, for example, those receiving 10 or more regular medicines, or those receiving 4 to 9 regular medicines together with other unfavorable factors like a contraindicated drug [8].

Polypharmacy has a negative impact on the elderly patients affecting both their physical and mental well-being [9]. Negative clinical consequences include the high healthcare costs to both patients and healthcare system by the inconvenient medication prescribing, hospitalization, and increased outpatient's visits [10]. Some elderly patients might switch between physicians, which usually contributes to drug-drug interactions, while other patients consume medication without prescriptions and physicians' consultation, which leads to additional harmful adverse drug reactions [10].

The burden of medication referred to adapting challenges when living with high number of medicines; acts of managing the hassle and conflict of medicines, and strategies to solve challenges of routines [9]. Elderly patients carry a high burden of illness for which medications are prescribed, along with increased risk of adverse drug reactions [9]. Many tools are available to measure treatment-related burden such as Medicines Questionnaire (BMQ), the Treatment Satisfaction Questionnaire for Medication (TSQM), and the Treatment Burden Questionnaire (TBQ) [15]. The LMQ-3 is a validated UK questionnaire to determine drug burden based on demographic and pharmacologic principles [13].

Decreased functional capacity associated with a remarkable decline in the ability to perform instrumental activities of daily living and decreased physical functioning are all contributing to the burden of taking multiple drugs [10]. Non-adherence is a widespread issue and is usually associated with complicated medication regimens, potential disease progression, treatment failures, hospitalization, and adverse drug events which could be life-threatening [10]. Medication adherence along with medication burden demonstrates a challenge and is considered a complicated situation that requires management [11]. Communication is the key when it comes to dealing with polypharmacy, especially when a new medicine is initiated, new medicine is added to the regimen or when the patient transfers to another health-care setting [11].

This study aims to assess medication-related burden among Bahraini elderly in relation to their medication consumption patterns and other socio-demographic characteristics and identify specific issues that need to be addressed by the responses using LMQ-3 and semi-structured interview. The fact of such a study being the first of its kind in Bahrain represents an excellent opportunity to shed light on the use of medicines in the elderly community in the kingdom of Bahrain and the burden associated with it.

Methods

Study design

Descriptive/analytical cross-sectional study which is a part of the graduation project for the B.Sc. in Pharmacy at the College of Health and Sport Sciences at the University of Bahrain that was conducted on 500 individuals aged 65 years and over taking five or more prescription medicines. Ethical approval of the project was obtained from the Pharmacy at the College of Health and Sport Sciences at the University of Bahrain.

Inclusion and exclusion criteria

The study included members of the public aged 65 years of age and over. The participants had at least one chronic disease and use at least five prescription medicines (POM). Patients suffering from life-threatening or terminal disease were excluded from the study along with those suffering of any kind of mental disorders or cognitive impairment. Patients who are unwilling to participate were excluded from the study as well.

Sample size calculation

The sample size was determined according to Slovin's formula [12] using the equation $n = N / (1 + N \times e^2)$, where $N = 45118$ is the population of the elderly aged 65 and over in Bahrain, and e value which is 0.05 denotes the allowed probability of committing an error in selecting a sample from the population at 95% confidence interval. Therefore, the ideal sample size was 397 although recruiting 500 respondents was considered even distribution between the group members.

The survey tool

A questionnaire along with semi-structured interviews was used to collect the required data. The semi-structured interviews included general questions about each patient's health status and any current difficulties encountering them with medication. The living with medicines questionnaire-3 (LMQ-3) was used from the original developers at University of Kent after obtaining the approval from the authors [13]. A translated version was used in Arabic after receiving approval from the original developers [14]. The LMQ-3 includes 40 Likert-type statements (strongly agree to strongly disagree), a Visual Analog Scale, a free-text question, and background characteristic. LMQ-3 consists of eight-domain scales to assess patients' attitudes about the medicines burden. The domains include Relationships/Communication with health professionals about medicines, Practical difficulties, Cost-related burden, Side effect burden, Lack of effectiveness, Attitudes/Concerns about medicine use, Impact on/Interference in day-to-day life, and Control/Autonomy to vary regimen. Each domain is assessed with a specific number of items and a total score is computed from all items. A summated rating scale format is used with five choices per item ranging from "strongly disagree" to "strongly agree". Reverse scoring is used for negatively worded questions where higher scores reflect a higher

burden experience of medicine use. Domain scores can then be calculated by summing the scores for the statements included in each of the eight domains. Total LMQ scores is the sum of all domain scores and range from 40 – 200. The degree of the burden is categorized as: minimal (scores of 40–87), moderate (88–110) and high (≥ 111 , potentially benefiting from intervention), based on the data from an English population. The tool was adapted for Bahrain in both English and Arabic by modifying the questions with issues of cultural differences, removing the list of ethnic groups, and adding two more questions that involved the use of over the counter and herbal supplements along with prescription medicines to explore this aspect and also due to popular use of herbal medicines by the local population.

Survey distribution

To ensure a diverse study population and wider access to the study, an approach of Convenience Non-Random Sampling Design to survey distribution was used (i) via hospitals, (ii) via health-centers, and (iii) via clinics, and community pharmacies.

We (the investigators) planned different visits from November 2020 to December 2020. During the rounds, we screened participants for eligibility, explained the study aim, obtained participants' verbal consent and provided a direct copy of the survey or a QR code for the website link based on each participant's preference. Most of the participants were fully respondents to the LMQ-3. However, any missing value from the respondents were replaced by the median score of the scale.

Data entry and analysis

SPSS 23 was used for data entry and analysis. Frequencies and percentages were computed for the categorical variable. Mean and standard deviation were computed for the quantitative variable. LMQ-3 scores were compared by participant characteristics using independent t-tests or One-way analysis of variance (ANOVA). Independent samples t-test was used to determine whether there is a significant difference in mean scores between two groups. ANOVA test was used to determine whether there is a significant difference in mean scores between more than two groups. In both statistical tests, p-value of less than 0.05 was considered statistically significant. In a domain analysis, participants' responses to statements were categorized according to the number which indicated they "strongly agree/agree" OR "strongly disagree/disagree" OR had a neutral opinion. Unanswered statements in any questionnaire were replaced by a neutral answer. The mean scores for each domain were compared by participant characteristics and divided by the maximum possible domain score to derive a "percentage maximum score". We hypothesized that medicine burden may be associated with gender, age, employment, education level, type of medicines used, the number or frequency of medicines used, requiring assistance with medicines use, or paying for prescription medicines.

Data were examined for associations between these possible predictors and dependent variables (LMQ3 scores, domain scores).

Overall burden

The overall burden was calculated by summing up the mean scores of all the domains which turned out to be 126.2, divide it by 200 (the maximum burden score) and then multiply it by 100. Final burden was 63% which is categorized as high burden.

Results

Participants

The study included a total of 500 survey responses. Most of the responses were submitted from patients who visited hospitals and health centers. The other portion of responses were taken from patients who visited clinics and community pharmacies. Most commonly, participants were

female (50.4%), 65 - 69 years old (63.4%), retired (58.7%), and educated at school (60.8%) (Table I).

The majority of the patients (76%) preferred the contactless method via scanning the QR code and answering the questions on the website instead of answering into a direct copy of the survey to comply with the COVID-19 pandemic precautions.

Reliability

Scale reliability for the eight LMQ-3 domains was tested using Cronbach's alpha (Table II). The general rule of thumb is that a Cronbach's alpha of 0.70 and above is good, 0.80 and above is better, and 0.90 and above is the best. Most of the domains came with results higher than 0.70 and 0.80 with a general LMQ result of 0.91 which demonstrates the reliability and solidity of the research. The value of 0.686 was also found to be acceptable by our statistician as it is very close to the desired value of 0.7.

Table I. Participant Characteristics.

Characteristics		n (%)
Number of medicines	5 - 6	268 (53.6)
	7 - 8	153 (30.6)
	≥9	79 (15.8)
Type of medicines	Tablets/Capsules	254 (50.8)
	Others	4 (0.8)
	Tablets/Capsules and others	242 (48.4)
Frequency of medicine use	Once daily	24 (4.8)
	Twice daily	127 (25.4)
	Three times daily	328 (65.6)
	Four times daily	21 (4.2)
Pays for prescriptions	Yes	47 (9.4)
	No	453 (90.6)
Requires help with medicines use	Yes	213 (42.6)
	No	287 (57.4)
Person provides help	Husband/Wife	127 (60.2)
	Relative	76 (36)
	Healthcare professional	8 (3.8)
Gender	Male	248 (49.6)
	Female	252 (50.4)
Age	65 - 69	317 (63.4)
	70 - 74	102 (20.4)
	≥75	81 (16.2)
Highest level of education	School	304 (60.8)
	Technical College/Apprenticeship	97 (19.4)
	University	97 (19.4)
	Other	2 (0.4)
Employment status	Employed	38 (7.6)
	Unemployed	166 (33.3)
	Retired	293 (58.7)
	Full-time student	2 (0.4)

Table II. Reliability of Domains and LMQ.

Domains	Cronbach's Alpha
Relationships/Communication with health professionals about medicines	0.686
Practical difficulties	0.765
Cost-related burden	0.760
Side effect burden	0.871
Lack of effectiveness	0.647
Attitudes/Concerns about medicine use	0.822
Impact/Interference to day-to-day life	0.851
Control/Autonomy to vary regimen	0.779
LMQ	0.914

Most commonly prescribed medications

The top five medicines used by participants in Bahrain included Metformin HCL 500-1000 mg as the most used medicine (57%), the second most used medicine was Acetylsalicylic acid 81 mg (48.6%), the third most used medicine was Gliclazide 60 mg (44.4%), the fourth most used medicine was Bisoprolol 2.5-5 mg (30.2%) and the fifth most used medicine was Perindopril 5-10 mg (29%) (Table III).

Table III. Most Prescribed Medications in Bahrain.

Medications	n (%)
1. Metformin HCL 500-1000mg	285 (57)
2. Acetylsalicylic acid 81mg	243 (48.6)
3. Gliclazide 60mg	222 (44.4)
4. Bisoprolol 2.5-5mg	151 (30.2)
5. Perindopril 5-10mg	145 (29)
6. Atorvastatin 20-40mg	143 (28.6)
7. Levothyroxine 25-100mcg	143 (28.6)
8. Valsartan 80-160mg	132 (26.4)
9. Amlodipine 5mg	127 (25.4)
10. Valsartan/hydrochlorothiazide 80-160/12.5	119 (23.8)
11. Insulin Glargine	103 (20.6)
12. Rosuvastatin 10mg	97 (19.4)
13. Simvastatin 20mg	96 (19.2)
14. Omeprazole 20mg	93 (18.6)
15. Insulin Aspart	89 (17.8)
16. Perindopril/indapamide 5/1.25mg	86 (17.2)
17. Tamsulosin 0.4mg	85 (17)
18. Perindopril/amlodipine 5/5mg	84 (16.8)
19. Escitalopram 10mg	81 (16.2)
20. Indapamide 1.5mg	60 (12)
21. Esmeprazole 20mg	54 (10.8)
22. Sitagliptin 100mg	50 (10)

LMQ scores

LMQ-3 scores were normally distributed. The mean score was 126.2 (SD=20.9). Overall, participants had no/minimal burden (0.4%, scores=40-87), moderate burden (27.4%, scores=88-110), or a high degree of burden (72.2%, score \geq 111). The highest mean scores/burden were in participants using medicines four times daily (M=147.2).

The highest negative individual responses indicated that (90.2%) were concerned about forgetting to take their medicines (84.6%) (Table IV). The top three percentage maximum domain scores were for Concerns (79.1%), Side effects (72%), and Impact on/Interference in day-to-day life (68.4%) (Table V).

Domain analysis

There were significant differences in mean scores by participant characteristics that were noticed in the number of medicines used, type of medicines and employment statuses in LMQ-3 and all domains. Being a graduate of technical college was associated with having a high burden in six of the eight domains (all except lack of effectiveness and autonomy) and being \geq 75 years-old in all seven domains (all except autonomy) (Table V).

Overall burden

VAS (Visual Analog Scale) scores showed significant differences in mean scores by participant characteristics. The highest mean scores/burden were seen in \geq 75 years-old age group (7.7, $p<0.001$) and the lowest mean scores/burden was seen in the frequency of once and twice daily, respectively (5.5, 5.3, $p<0.001$) (Table VI).

Pharmacy

Table IV. Domain Analysis. Responses to Statements.

Statements	Agree	Neutral	Disagree
	n (%)	n (%)	n (%)
1: Relationships/Communication with health professionals about medicines (Items = 6, Mean (SD) = 15.6 (3.8))			
I trust the judgment of my doctor(s) in choosing medicines for me	354 (70.9)	55 (11)	90 (18)
My doctor(s) listen to my opinions about my medicines	330 (66.1)	48 (9.6)	121 (24.2)
My doctor(s) takes my concerns about side effects seriously	354 (70.8)	67 (13.4)	79 (15.8)
I get enough information about my medicines from doctor(s)	308 (61.6)	34 (6.8)	158 (31.6)
I notify my doctor/pharmacist before starting to take any herbal supplements, traditional medicines or multiple vitamins	184 (36.8)	48 (9.6)	268 (53.6)
The health professionals providing my care know enough about me and my medicines	301 (60.4)	59 (11.8)	138 (27.7)
2: Practical difficulties (Items = 7, Mean (SD) = 22.4 (5))			
I find getting my prescriptions from the doctor difficult	42 (8.4)	31 (6.2)	425 (85.3)
I find getting my medicine from the pharmacist difficult	260 (52.1)	21 (4.2)	218 (43.7)
I am comfortable with the times I should take my medicines	313 (62.6)	39 (7.8)	148 (29.6)
I am concerned that I may forget to take my medicines	451 (90.2)	19 (3.8)	30 (6)
It is easy to keep to my medicines routine	198 (39.6)	47 (9.4)	255 (51)
I find using my medicines difficult	287 (57.6)	39 (7.8)	172 (34.5)
I have to put a lot of planning and thought into taking my medicines	286 (57.2)	28 (5.6)	186 (37.2)
3: Cost-related burden (Items = 3, Mean (SD) = 9.2 (3.1))			
I worry about paying for my medicines	346 (69.5)	23 (4.6)	129 (25.9)
I sometimes have to choose between buying basic essentials or medicines	130 (26.2)	89 (17.9)	277 (55.8)
I have to pay more than I can afford for my medicines	132 (26.7)	97 (19.6)	266 (53.7)
4: Side effect burden (Items = 3, Mean (SD) = 10.8 (3.1))			
The side effects I get are sometimes worse than the problem for which I take medicines	252 (50.4)	73 (14.6)	175 (35)
The side effects I get from my medicines interfere with my day-to-day life (e.g. Work, housework, sleep)	325 (65.3)	102 (20.5)	71 (14.3)
The side effects I get from my medicines adversely affect my well-being	288 (57.6)	110 (22)	102 (20.4)
5: Lack of effectiveness (Items = 6, Mean (SD) = 14.4 (3.2))			
I am satisfied with the effectiveness of my medicines	351 (70.2)	51 (10.2)	98 (19.6)
My medicines prevent my condition getting worse	407 (81.4)	72 (14.4)	21 (4.2)
My medicines live up to my expectations	350 (70)	105 (21)	45 (9)
My medicines allow me to live my life as I want to	309 (62)	107 (21.5)	82 (16.5)
My medicines are working	359 (71.9)	86 (17.2)	54 (10.8)
The side effects are worth it for the benefits I get from my medicines	263 (52.6)	105 (21)	132 (26.4)
6: Attitudes/Concerns about medicine use (Items = 7, Mean (SD) = 27.7 (5.4))			
I worry that I have to take several medicines at the same time	374 (74.8)	24 (4.8)	102 (20.4)
I would like more say in the brands of medicines I used	398 (79.8)	56 (11.2)	45 (9)
I feel I need more information about my medicines	422 (84.6)	14 (2.8)	63 (12.6)
I am concerned about possible damaging long term effects of taking medicines	357 (71.5)	33 (6.6)	109 (21.8)
I am concerned that I am too reliant on my medicines	383 (76.8)	51 (10.2)	65 (13)
I worry that my medicines may interact with each other	374 (74.8)	27 (5.4)	99 (19.8)
I am concerned that my medicines will interact with my herbal supplements/ traditional medicines or types of food	306 (61.2)	32 (6.4)	162 (32.4)
7: Impact/Interference to day-to-day life (Items = 5, Mean (SD) = 17.1 (4.6))			
My medicines interfere with my social or leisure activities	307 (61.4)	86 (17.2)	107 (21.4)
My medicines interfere with my sexual life	224 (44.8)	167 (33.4)	109 (21.8)
Taking my medicines affects my driving	201 (40.4)	58 (11.6)	239 (48)
My medicines interfere with my social relationships	247 (49.4)	98 (19.6)	155 (31)
Taking my medicines causes me problems with daily tasks (such as work, housework, hobbies)	274 (54.8)	92 (18.4)	134 (26.8)
8: Control/Autonomy to vary regimen (Items = 3, Mean (SD) = 9 (2.9))			
I can vary the dose of the medicines I take	220 (44)	47 (9.4)	233 (46.6)
I can choose whether or not to take my medicines	210 (42.1)	58 (11.6)	231 (46.3)
I can vary the times I take my medicines	176 (35.2)	80 (16)	244 (48.8)

Table V. Mean Domain Scores and Mean LMQ Scores by Participant Characteristics.

Characteristics	Relationships Max score = 30	Difficulties Max score = 35	Cost Max score = 15	Side effect Max score = 15	Lack of Effect Max score = 30	Concerns Max score = 35	Interference Max score = 25	Autonomy Max score = 15	LMQ Max score = 200
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Number of medicines									
5 - 6	14.6 (3.2)	20.9 (4.2)	8.5 (2.7)	10.1 (2.5)	14 (2.6)	26.3 (4.9)	15.3 (3.6)	9.5 (2.8)	119.2 (14.9)
7 - 8	16.2 (4.2)	23 (5.7)	9.5 (3.3)	10.9 (3.5)	14.7 (3.2)	28.2 (5.7)	18.4 (4.9)	8.8 (2.8)	129.7 (24.8)
≥9	17.9 (3.6)	26 (4.2)	10.8 (3.1)	13.4 (2.5)	14.9 (4.5)	31.7 (4)	20.9 (4.1)	7.9 (2.8)	143.5 (18.5)
P-value ^b	<0.001	<0.001	<0.001	<0.001	0.036	<0.001	<0.001	<0.001	<0.001
Type of medicines									
Tablets/Capsules	14.5 (3.1)	20.6 (4.1)	8.7 (2.6)	10 (2.8)	14 (2.9)	26.4 (4.4)	15.6 (3.9)	9.4 (2.8)	119.3 (15.8)
Tablets/Capsules and others	16.8 (4.1)	24.2 (5.3)	9.7 (3.4)	11.7 (3.2)	14.6 (3.4)	29.1 (5.9)	18.7 (4.8)	8.5 (2.8)	133.5 (23.2)
P-value ^a	<0.001	<0.001	<0.001	<0.001	0.038	<0.001	<0.001	0.001	<0.001
Frequency of medicine use									
Once daily	16 (2.6)	17.4 (3.4)	9.5 (4.1)	9.4 (2.4)	13.7 (3)	22.4 (4.1)	13.4 (4.2)	10.3 (2.5)	112 (13.7)
Twice daily	15.4 (3.6)	19.9 (3.7)	7.6 (2.8)	9.5 (2.7)	14.4 (2.6)	24.3 (4.5)	14.4 (3.9)	10.4 (2.5)	116 (14.9)
Three times daily	15.5 (3.9)	23.4 (5)	9.6 (2.8)	11.3 (3.1)	14.3 (3.3)	29.1 (4.9)	18.2 (4.3)	8.5 (2.8)	129.9 (20.9)
Four times daily	19 (3)	26.5 (5)	12.4 (2.1)	12.9 (3)	15.8 (3.5)	32 (4.7)	20.6 (4.9)	8 (2.6)	147.2 (23.8)
P-value ^b	<0.001	<0.001	<0.001	<0.001	0.122	<0.001	<0.001	<0.001	<0.001
Pays for prescriptions									
Yes	16.1 (4.1)	22.9 (4.7)	11 (2.5)	11.8 (2.2)	15.4 (3.8)	29 (4.7)	17.4 (4.1)	8.9 (2.5)	132.5 (16.1)
No	15.6 (3.8)	22.3 (5.1)	9 (3.1)	10.7 (3.1)	14.2 (3.1)	27.6 (5.4)	17.1 (4.7)	9 (2.9)	125.6 (21.3)
P-value ^a	0.338	0.451	<0.001	0.004	0.021	0.051	0.693	0.818	0.008
Requires help with medicines use									
Yes	17.1 (3.7)	24.2 (5)	9.2 (3.5)	11.9 (3)	15.1 (3.6)	29.3 (5.6)	18 (5.1)	9.9 (2.8)	134.6 (20.7)
No	14.6 (3.5)	21 (4.6)	9.2 (2.7)	10 (2.9)	13.8 (2.7)	26.6 (4.9)	16.5 (4.2)	8.3 (2.7)	120 (18.9)
P-value ^a	<0.001	<0.001	0.873	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Person provides help									
Husband/Wife	16.9 (3.6)	25.5 (4.7)	9.9 (3.2)	12.6 (2.6)	15.5 (3.7)	30.7 (4.4)	19.4 (4.9)	9.2 (2.9)	139.7 (19.8)
Relative	17.6 (4)	21.9 (5)	8.2 (3.7)	10.7 (3.6)	14.3 (3.3)	26.7 (6.7)	15.9 (4.9)	11.1 (2.3)	126.4 (20.7)
P-value ^a	0.201	<0.001	0.001	<0.001	0.023	<0.001	<0.001	<0.001	<0.001
Gender									
Male	13.7 (2.7)	20.4 (4.1)	8.6 (2.3)	9.9 (2.3)	13.8 (2.3)	26.2 (4.1)	16 (3.4)	8.8 (3)	117.2 (14.3)
Female	17.6 (3.8)	24.3 (5.1)	9.8 (3.5)	11.8 (3.4)	14.9 (3.7)	29.2 (6)	18.3 (5.4)	9.2 (2.7)	135.1 (22.6)
P-value ^a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.083	<0.001
Age									
65 - 69	14.8 (3.6)	21.3 (4.5)	8.9 (2.8)	10.4 (2.7)	14.1 (2.8)	26.8 (5.1)	16.2 (4.2)	9 (2.7)	121.5 (18.1)
70 - 74	15.9 (3.9)	23.4 (4.8)	9.3 (3.2)	11 (3.3)	14.4 (3)	28.3 (5.2)	17.8 (4.7)	9 (3.3)	129.2 (21.4)
≥75	18.6 (2.9)	25.3 (5.8)	10 (3.7)	12.3 (3.6)	15.3 (4.4)	30.4 (5.8)	20.1 (5)	9 (2.8)	141 (23.1)
P-value ^b	<0.001	<0.001	0.014	<0.001	0.011	<0.001	<0.001	1.000	<0.001
Highest level of education									
School	14.5 (3.3)	20.7 (4.1)	8.4 (2.8)	9.6 (2.7)	14.1 (2.8)	25.9 (4.8)	15.9 (3.9)	9.1 (3)	118.2 (16.6)
Tech	18.1 (3.5)	26.9 (3.6)	10.5 (3)	13.3 (2)	14.9 (3.8)	31.8 (4)	19.9 (4.5)	8.7 (3)	144 (17.3)
University	17 (4)	23 (6.1)	10.1 (3.2)	12.3 (3)	14.5 (3.6)	29.2 (5.6)	18.3 (5.4)	9.2 (2.2)	133.6 (22.9)
P-value ^b	<0.001	<0.001	<0.001	<0.001	0.093	<0.001	<0.001	0.423	<0.001
Employment status									
Employed	17 (3.6)	26.1 (4)	11.6 (2.9)	13 (2.6)	14.2 (4.1)	31.7 (4.1)	18.7 (5.6)	9.2 (2.9)	141.5 (18.8)
Unemployed	17.6 (3.9)	24.1 (5)	9.1 (3.6)	11.2 (3.6)	15.3 (3.5)	28.3 (6.3)	17.6 (5.4)	9.7 (2.6)	132.8 (23.9)
Retired	14.3 (3.3)	21 (4.6)	8.9 (2.6)	10.3 (2.6)	13.8 (2.7)	26.9 (4.6)	16.7 (3.9)	8.6 (2.9)	120.5 (17.1)
P-value ^b	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.010	<0.001	<0.001

Notes: ^aIndependent samples t-test; ^bAnalysis of variance (ANOVA). Full domain names: 1: Relationships/Communication with health professionals about medicines, 2: Practical difficulties, 3: Cost-related burden, 4: Side effect burden, 5: Lack of effectiveness, 6: Attitudes/Concerns about medicine use, 7: Impact/Interference to day-to-day life, 8: Control/Autonomy to vary regimen. Abbreviation: Tech: Technical College/Apprenticeship.

Table VI. Overall burden of medicines by participant characteristics.

Characteristics	Overall burden		P-value
	Mean (SD)		
Number of medicines	5 - 6	5.6 (1.9)	<0.001 ^b
	7 - 8	7 (2.1)	
	≥9	7.4 (2.4)	
Type of medicines	Tablets/Capsules	5.7 (2.1)	<0.001 ^a
	Tablets/Capsules and others	7 (2.1)	
Frequency of medicine use	Once daily	5.5 (3.1)	<0.001 ^b
	Twice daily	5.3 (1.9)	
	Three times daily	6.7 (2)	
	Four times daily	7.5 (2.7)	
Pays for prescriptions	Yes	7.1 (2.2)	0.011 ^a
	No	6.2 (2.2)	
Requires help with medicines use	Yes	6.9 (2.3)	<0.001 ^a
	No	5.9 (2)	
Person provides help	Husband/Wife	7.2 (2.6)	0.022 ^a
	Relative	6.5 (1.7)	
Gender	Male	5.7 (1.8)	<0.001 ^a
	Female	7 (2.4)	
Age	65 - 69	6 (1.9)	<0.001 ^b
	70 - 74	6.3 (2.3)	
	≥75	7.7 (2.5)	
Highest level of education	School	5.9 (1.8)	<0.001 ^b
	Technical College/Apprenticeship	7.5 (2.3)	
	University	6.6 (2.7)	
Employment status	Employed	7 (2.4)	<0.001 ^b
	Unemployed	6.9 (2.2)	
	Retired	5.9 (2.1)	

Notes: ^aIndependent samples t-test; ^bAnalysis of variance (ANOVA).

Discussion

The findings offer insight into the medicine burden in terms of numbers, formulations and complexity of medicines prescribed for the elderly population using more than 5 medicines in Bahrain and into the aspects affecting every patient's perception of this burden. Four major diseases (diabetes mellitus, hypertension, cardiovascular and gastro-intestinal) constituted the large majority of prescribed medicines, and within four of these groups, patients were prescribed an average of at least five medicines, but could receive up to fourteen different medicines which indicated the widespread prevalence of polypharmacy all over Bahrain.

The present study, using the LMQ-3, found a wide range of medicines burden among participants in Bahrain, with the majority of participants having high burden. In contrast, participants in New Zealand experienced minimal to moderate burden in over two-thirds of participants to high burden in almost a third [15]. Other factors playing a role in the medicine's burden are the number of medicines

used and higher frequency of administration as these could create complicated medicine regimens for some patients.

The domain analysis suggested the main drivers of burden were: (i) concerns about medicine use (ii) side effect burden, and (iii) interference in day-to-day life. The Concerns about multiple medicine use domain contributed to the highest medicine burden percentage, which was an important factor in the present study and others [16-18]. Prescribers and pharmacists could address medicine burdens with practical advice, by asking patients about their medicine use or look at their LMQ-3 responses to identify their concerns. Identifying and addressing elderly patients' fears might help improve poor adherence and optimize health outcomes [19]. On the other hand, the lack of effectiveness domain had the lowest medicine burden percentage, which is considered as a moderate burden where older people described the satisfaction level of their medication's effectiveness. Most of the participants felt that medicines were preventing their condition from worsening, allowed them to live their life as they want to, and they

would handle the side effects for the benefits they are obtaining from their treatment regimens.

The findings indicated a significantly higher burden in specific participant characteristics including employed patients due to the imbalance between working and using the medicines, technical colleges graduates as they need more physical effort and energy, ≥ 75 years old as the increased age carries more burden and risks to the patients, using ≥ 9 medicines and using medicines four times a day which contribute to inconvenient treatment regimens and risk of incompliance. Furthermore, living through the COVID-19 crisis and witnessing the terrible loss of many of the older adults highlighted the sensitivity of the ageing population and the extreme attention needed to be given to their health needs. Physicians and other health-care professionals should work together to develop interventions on these groups, to reduce their medicines burden and help them get the best out of their medicines [20].

It is increasingly important to obtain the patients perspective on medicine burden and to learn more about its association with medicine-compliance behavior. This present study showed that medicine complexity may be related to compliance. Minority of patients (198 Out of 500) stated that it was easy to keep their medicines routine which indicated the high burden felt by most of the patients in adhering to their medicines' regimens.

The findings indicate relatively high prevalence of polypharmacy ranging from the use of 5-6 medicines as the majority (53.6%), 7-8 medicines as the minority (30.6%) and ≥ 9 medicines as the remainder, despite the increasing awareness of drug adverse effects and multidrug use. Other studies showed a high prevalence of polypharmacy in GCC (Gulf Cooperation Council) countries such as Qatar 75.5% [21] and Kuwait 68.6% [22]. A Korean study reported higher polypharmacy prevalence among elderly population, i.e. up to 86.4% [23]. In addition, polypharmacy prevalence increased with age, as shown in table V. Furthermore, through aging and the progression of chronic diseases, management tends to be more intensive including several medication and additional doses administration. That might be justified by our findings as participants using medicines four times daily had the highest mean scores/burden and those taking medicines once daily, had the lowest scores.

An association between endocrine/cardiovascular diseases and the use of a large number of medicines has been established in previous studies [24]. In the present study, Anti-diabetic agents were the most used by participants, including Metformin HCL and Gliclazide. This may be accounted for by the increasing incidence of diabetes mellitus cases in Bahrain. Extensive attention should be given for diabetic patients to reduce acute and chronic disease complications such as cardiovascular disease, stroke, retinopathy, and peripheral vascular disease by reviewing their prescription medicines regularly, improving the level of sugar control and other physical and

biological indicators in the blood such as BMI (body mass index), blood pressure, urea, and fats. Diabetic patients should be encouraged to adhere to their treatment plans and follow preventive medical services including vaccinations and regular retina and foot screening [25].

It is worth mentioning that participants who found that getting their prescriptions from the doctor is difficult were of a low percentage. In contrast, participants who found that getting their prescriptions from the pharmacists is difficult were of a high percentage. The differences in percentages might be an indicator of the pharmacists' rigidity when they face any interactions, wrong medication choices or any other reason the doctors were not aware of. In contrast, there was a better level of general understanding of the pharmacist's role in Canada [26]. Cautious and alert pharmacists who are able to hinder the dispensing process when needed would definitely help reduce medication errors and adverse drug reactions, thus saving the elderly patient from potential harm [27].

Harm can reach the patients from other sources that are accessible and reachable such as herbal supplements, traditional medicines, and even multivitamins. The percentage of participants who usually notify their doctor or pharmacist before starting any herbal/traditional supplements and vitamins was extremely low compared to the majority of participants who do not notify their doctor or pharmacist before starting any herbal/traditional supplements and vitamins which is supported by previous studies [28,29]. Physicians and pharmacists must always guide the patients on the importance of reporting any new supplement or OTC (over-the-counter medicines) that are used by them. Additionally, emphasizing to the patients their need to consult their physicians or the pharmacists before starting any new medicine can result in less adverse drug reactions and potential threat [30].

From LMQ scores, this study found significant differences in mean scores in both genders. Females had a higher burden rate than males overall LMQ and domains (except domain 8: Lack of effect and Autonomy). The differences between males and females can be related to the differences in the psychological nature of both sexes and are due to a complex association of biological, developmental and cultural factors. In contrast, a study done in New Zealand using the LMQ-3 questionnaire indicated no significant differences between male and female mean scores which can be contributable to the cultural differences between Bahrain and New Zealand [15].

According to the results of the employment statuses, the employed had higher LMQ-3 scores/burden compared with other subcategories. This might be attributable to the overload burden on the employed elderly and the challenges facing them on a daily basis. Trying to balance between their jobs and the use of multiple medications is difficult and needs further modifications in the elderly patients' regimens. In the second place, unemployment comes with

a high LMQ-3 score/burden as well. Unemployment may be a reason or consequence of poor health and it has been linked to medicine burden [31]. The present study and other studies examining medicine burden suggest that unemployed group needs more encouragement and support with medicine use. As expected, the retired had recorded the lowest mean scores/burden in the employment field and might be a result of participants having more time to focus on medicine-related tasks.

Not surprisingly, the frequent use of medicines including three times daily and four times daily showed associations with higher LMQ-3 scores and burden compared to other frequencies of medicine use.

Furthermore, participants using medicines four times a day had the highest LMQ-3 scores in their group and in four domains (Relationships, Practicalities, Concerns, Interference). An awareness of regimen complexity is also important when it comes to prescribing or reviewing medicines.

Our findings showed an association between the number of medicines used and the burden felt on the elderly, as the number of medicines increased the mean scores increased and thus, the burden on the elderly which explains why participants using ≥ 9 medicines had the highest LMQ-3 score in their sub-group. Similar findings were seen in the New Zealand study for high and frequent users of medicines as ≥ 10 medicines had the highest LMQ-3 score in their sub-group. Additionally, participants using medicines ≥ 4 times a day had the highest LMQ-3 scores in their sub-group [15].

This study also found some variation in perceptions of medicine burden between patients requiring help with medicine use and patients who don't. Elderly patients who require assistance from a spouse or relative had higher mean scores/burden in all domains (except cost-related burden domain) where adhering to complex treatment regimens proved challenges for some elderly patients and impacted on their independence. Similar to the findings, Participants in New Zealand requiring help using medicines had the highest mean LMQ-3 scores/burden ($M=116.0$), and close to those in UK studies ($M=116.4$) [32,33]. Furthermore, the help from a husband/wife had a significant LMQ-3 score/burden compared to the help obtained from a relative. These differences draws attention to the high burden of using multiple medications where they do not only exert their effects on patients' physical health but also affect their mental well-being, as many marital relationships can be lost and damaged when the patients start feeling that their medication are standing between them and their personal life [34].

From the LMQ scores, this study found significant differences in mean scores/burden between patients who pay for their prescriptions and patients who do not pay for their prescriptions. These differences in the mean scores

might be an indicator of the financial burden associated with patients who pay for their prescriptions. Low-income patients or the absence of health insurance may eventually lead to poor health outcomes and non-adherence. High medication costs for complex, multi-morbid patients may leave low-income patients in a difficult health situation [35,36]. Patients may discontinue the treatment due to their limited financial resources that are needed to cover other basic life necessities such as paying for the bills or rent [35,36]. The elderly population is at a higher risk of multi-morbidity and therefore higher medication costs. Poor adherence because of financial issues might ultimately lead to a higher risk of adverse reactions and poor health outcomes [37].

The strength of the present study is that it used a validated survey tool which is the LMQ-3. Response rates were excellent where the majority was found in hospitals and health centers. Responses were from 248 males and 252 females; it covered three age groups and three levels of education. Moreover, study numbers were sufficient to detect significant differences. This study has some limitations. We interviewed some patients via the phone to recruit community dwelling elderly because this population is difficult to reach, specifically during the COVID-19 pandemic. Other limitations may be related to inaccuracy in recording dietary supplements, thus resulting in the underestimation of the true prevalence of polypharmacy. Another limitation is that the distribution of the collected responses (hospitals, pharmacies, by phone etc.) is not known.

Future studies should document potential herb-drug interactions among the elderly.

Conclusion

In conclusion, an extensive range of medicine burden was seen among study participants in Bahrain, with over two-thirds having a high degree of burden and almost a third, moderate burden. Additionally, no minimal burden was recorded in the study. Subgroups with high burden included those requiring help using medicines, the employed, females, ≥ 75 years-old, and high or frequent medicine users. Practitioners and pharmacists should spend more time discussing medicine burden with elderly patients to improve their medicine adherence and health outcomes. The LMQ tool could be beneficial in examining medicine burden in patients with multiple chronic diseases (e.g. diabetes mellitus and cardiovascular disease) as it addresses all aspects of the co-morbid challenges and associated burden with medicine use. Integration of the LMQ-3 in health-care system by practitioners, nurses and even clinical pharmacists would identify and address the burden issues of each patient and thus, facilitate in setting them on the best therapy regimen/plan that is designed for every individual's needs.

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