Saudi Pharmaceutical Journal 27 (2019) 208–219

Contents lists available at ScienceDirect

Saudi Pharmaceutical Journal

journal homepage: www.sciencedirect.com

Original article

Identifying treatment related problems and associated factors among hospitalized post-stroke patients through medication management review: A multi-center study

Iman A. Basheti [a,*], Shahnaz Mohammed Ayasrah [b], Muayyad Ahmad [c]

[a] Department of Clinical Pharmacy and Therapeutics, Faculty of Pharmacy, Applied Science Private University, Amman, Jordan
[b] Department of Applied Science, Al-Balqa Applied University, Al-Salt, Jordan
[c] School of Nursing, University of Jordan, Jordan

ARTICLE INFO

Article history:
Received 26 June 2018
Accepted 16 October 2018
Available online 19 October 2018

Keywords:
Medication management review
Pharmaceutical care
Treatment related problems
Stroke
Chronic conditions
Jordan

ABSTRACT

Background: Stroke is a major cause of disability and one of the leading causes of death among the elderly. Treatment related problems can lead to undesirable consequences. The Medication Management Review (MMR) service is aimed at identifying, resolving and preventing TRPs, subsiding the undesirable outcomes associated with TRPs.

Objectives: To explore the types, frequencies and severity of TRPs amongst post-stroke patients recruited through hospitals via conducting the MMR service by clinical pharmacists in Jordan. Associations between patient factors and the identified TRPs were explored.

Methods: This cross-sectional descriptive study was conducted over three months in 2017 in different geographical areas throughout Jordan. Randomly recruited patients were interviewed at the hospitals to collect their demographic data and clinical characteristics. Types/frequencies/severity of TRPs for each stroke patient were identified by a clinical pharmacist. Associations between the identified TRPs and patient's factors were explored through multiple regression analysis.

Key findings:

Out of 198 stroke patients (mean age: 56.6 ± 14.2) who completed the study, 110 (55.6%) were males. Many of the patients (82 (41.6%)) were smokers and 61 (69.2%) had hypertension and/or diabetes. The mean number of TRPs per patient was 2.5 ± 1.1. The most common TRP categories involved efficacy issues (198 (40.6%)), inappropriate drug adherence (136 (27.9%)) and inappropriate patient knowledge (114 (23.4%)). More than 70.0% (342/487) of the identified TRPs were of major severity. Higher number of TRPs was found to be associated with being a male, having a lower educational level, being a current smoker, having a higher number of drugs and a poorer quality of life.

Conclusion: Lack of drug efficacy, inappropriate drug adherence and patient knowledge were the major TRPs identified via delivering the MMR service to post-stroke patients. The identified TRPs highlights the importance of the MMR service, and supports planning future strategies aimed at decreasing the incidence of strokes.

© 2018 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Stroke is one of the leading causes of death and the major cause of disability among the elderly; it has been ranked as the third deadliest medical condition worldwide (Mozaffarian et al., 2016). According to the report of the World Health Organization, 15 million people worldwide suffer from a stroke every year. Of these, 5 million die and another 5 million are left permanently disabled, placing a burden on their family and community (World Health Organization. 2018). Stroke is associated with significant morbidity and mortality, a significant cause of long-term disability, and

* Corresponding author at: Faculty of Pharmacy, Applied Science Private University, Amman, Jordan.
E-mail addresses: Dr_iman@asu.edu.jo (I.A. Basheti), shahnazhamdan@bau.edu.jo (S.M. Ayasrah), mma4@ju.edu.jo (M. Ahmad).

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.jsps.2018.10.005
1319-0164/© 2018 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

exerts a significant burden on the economic state worldwide (Ehntholt & Yule, 2006).

Multimorbidity, defined as the presence of two or more long-term conditions, is becoming a challenge worldwide for patients, healthcare professionals and policy-makers (Barnett et al., 2012; Valderas et al., 2009). Hypertensive diabetic patients are at a substantially increased risk for primary and secondary strokes (McFarlane et al., 2005). Hypertension is a major risk factor for ischemic stroke and intracerebral hemorrhage (Straus et al., 2002). The crude incidence of stroke among patients with diabetes is three times greater than in the general population (Tuomilehto & Rastenyte, 1999). The presence of multiple chronic conditions are associated with higher number of medications and lower patient adherence, leading to a higher number of treatment-related problems (TRPs) (Basheti et al., 2016a).

A TRP has been defined as 'an event or circumstance involving patients' treatment that actually or potentially interferes with an optimum outcome for a specific patient' (AbuRuz et al., 2006). Many TRPs have been stated as preventable causes of morbidity and mortality, including hospital admissions for drug toxicity and fatal drug poisonings leading to death (de Freitas et al., 2018; Jonsson et al., 2009; Juurlink et al., 2003). It is important to recognize pharmaceutical services aimed at identifying, resolving and preventing TRPs, hence subsiding the undesirable clinical and economic outcomes associated with it (Altowaijri et al., 2013).

Studies revealed that patients with stroke are at a high risk to develop TRPs due to polypharmacy and Multimorbidity (Barnett et al., 2012; Gallacher et al., 2014). In addition, the psychological consequences of stroke, such as post-stroke anxiety and depression, can negatively affect the outcomes in patients with stroke (Rafsten et al., 2018; Shi et al., 2017), as it has been associated with decreased compliance with therapy, resumption of social activities and quality of life (Sturm et al., 2004; Williams et al., 2004). Such consequences may affect patient's adherence to recommended self-care activities (e.g. diet and exercise) and hence TRPs (Arowoiya et al., 2017).

Hence, identifying concurrent medical conditions and TRPs is an important priority for healthcare professionals to improve the management and health-related quality of life in stroke patients. Identifying TRPs for patients with stroke is essential to develop strategies for prevention, early detection, appropriate management and modifying treatments to individuals based on their needs, including cost, accessibility, and availability of medications, which in turn improved health outcomes (Hackett & Anderson, 2005).

The pharmacist has become an integral member of the multidisciplinary team providing clinical patient care in various healthcare settings (Basheti et al., 2016a, 2016b). Pharmacists' interventions in outpatient, inpatient, and emergency department settings have been shown to improve the control of modifiable risk factors (i.e. blood pressure, blood glucose and cholesterol levels) and reduce hospitalizations and mortality (Chisholm-Burns et al., 2010). Pharmacists' unique knowledge of pharmacology, pharmacokinetics and drug interactions makes them well-suited to assist stroke patients in maintaining a safe and effective use of medications with narrow margin of safety and with complex pharmacology and pharmacokinetics, such as anticoagulants (Lakshmi et al., 2013).

Medication Management Reviews (MMR) which are conducted by pharmacists have been an essential element of the expanded clinical services provided by pharmacists worldwide (Australian Government Medicare Australia; Laaksonen et al., 2010; The Royal Pharmaceutical Society, 2018). The MMR process utilizes the specific knowledge and expertise of each of the healthcare professionals involved; in the Australian model for example (Australian Government Medicare Australia), in collaboration with the general practitioner, a pharmacist comprehensively reviews the patient's medication regimen; after discussion of the pharmacist's report and findings, the doctor and patient agree on a medication management plan. With the patient being central to the development and implementation of this plan with their doctor, the MMR aims to maximize patients' care and benefit from their medications. The MMR service leads to positive clinical outcomes, including reduction in adverse drug events, severity of illnesses, healthcare service costs, and emergency department contacts (Basheti et al., 2013; Christensen & Lundh, 2013; Ramalho de Oliveira et al., 2010; Sorensen et al., 2004). The value of the MMR service has been demonstrated in previous published studies (Al Alawneh et al., 2018; Basheti et al., 2016a; Basheti et al., 2013; Basheti et al., 2017; Basheti et al., 2016b). It is reasonable to infer that through the MMR service, pharmacists can greatly benefit patients with post-stroke, identified right after their hospitalization and followed post hospital discharge.

In Jordan, pharmacists support the concept of pharmaceutical care, and patients show great satisfaction when a pharmaceutical care service is offered (Basheti et al., 2018; Elayeh et al., 2017). However, barriers to the broad implementation of pharmaceutical care have been reported, including suboptimal physician-pharmacist communication and inadequacies in pharmaceutical care training (Aburuz et al., 2012). Continuing professional development for pharmacists is not mandatory as yet, nor are there any post-licensure revalidation mechanisms in place (Bader et al., 2017). In spite of the introduction of the Pharm D programme in 2000, these concerns are still recognized, and have echoed in the hospital setting as well, where resistance to accepting or recognizing newer pharmacy clinical services still reported (Tahaineh et al., 2009). The MMR service is not effective in the country at present (Basheti et al., 2014; Qunaibi et al., 2013) limiting the scope of pharmacists to identify, prevent and resolve TRPs for post-stroke patients. Pharmacist's role in this area needs to be further explored in the different healthcare settings.

The aim of this study was to evaluate the types, frequencies and severity of the identified TRPs for hospitalized post-stroke patients via conducting the MMR service. Secondary aim includes exploring the association between patient factors (demographic data, clinical characteristics and quality of life) and the identified TRPs.

2. Methods

2.1. Study design and clinical setting

The study aims were addressed in a cross-sectional descriptive study design. Jordanian patients were recruited from multi-hospitals evenly distributed throughout Jordan. Nine major hospitals representing the three major health sectors in Jordan, including military, governmental, and educational hospitals (university teaching hospitals) were involved. Hospitals affiliated with these health sectors were divided according to their geographical area into three strata: the North, the Middle and the South of Jordan. Three hospitals representing the three chief sectors were then randomly selected from each stratum (the computer-generated randomization program was used (www.randomizer.org). Data collection occurred between April 2017 and June 2017.

2.2. Ethical approval

Ethical approval for the study was obtained from each ethical committee at the selected hospitals before conducting the study. A written informed consent was obtained from all patients after they were fully informed of the study purpose and objectives. All patients were assigned a code number to ensure confidentiality.

2.3. Inclusion criteria

All patients experiencing a first or succeeding ischemic or hemorrhagic stroke, and recently admitted to one of the selected hospitals, were included in the study. Stroke diagnosis was confirmed by a senior neurology specialist using computed tomography (CT) or magnetic resonance imaging (MRI). Inclusion criteria included patients diagnosed with stroke, 18 years or older, and willing to provide written informed consent.

2.4. Exclusion criteria

Patients diagnosed with subarachnoid hemorrhage or reversible neurovascular status (transient ischemic attack); because of differences concerning etiology, risk factors and management, patients diagnosed with a mental illness and/ or major psychiatric illness (such as dementia, confusion, psychosis and depression), patients with a history of taking psychotropic agents, patients having major hearing or visual difficulties, patients having a life-threatening or associated major illness (such as renal failure or cancer), and patients having speech impairment (such as aphasia) were excluded from the study.

2.5. Study protocol

Being an important part of the MMR service approach, a face-to-face interview using a structured questionnaire was used to collect data. The interviews were conducted by three trained research nurses (one from each geographical area) who were registered nurses and had at least 10 years of experience in providing care to stroke patients. Those nurses attended a four-days training program concerning the study purpose, questionnaire, protocol and strategies for conducting interviews. A pilot study with 15 patients (five patients from each stratum) was conducted with the attendance of one of the three principal researchers to assure the consistency in conducting the interviews. The patients' medical records were reviewed by the research nurse and the research coordinator (head nurse of the neuro-intensive care units or the head nurse of the medical floor) to determine patient eligibility and to collect information concerning co-morbidities, recent laboratory results, drug history (ceased medications), past medical and surgical history.

2.6. Study tools

A two-part questionnaire was used to collect data. The first part included information related to patient socio-demographic characteristics (i.e. age, gender, and marital status), personal characteristics (i.e. residential status and smoking) and stroke-related complications, such as the presence of dysphasia, visual problems and the ability to perform activities of daily living without any help.

The second part included questions based on a pre-printed published template (AbuRuz et al., 2006) used to collect the medical data including current medications, drug doses and therapeutic regimen. Patients were asked if they agree to receive a follow-up home visit by the clinical pharmacist following discharge from hospital to complete the MMR service.

Patient's physician was the medical doctor specialist (e.g. neurology specialist) that the patient was visiting for regular management of his or her medical condition/s. Physicians were contacted by the research team only in case a life threatening/major TRP was identified or if vital information regarding patient's health status was needed.

2.7. Self-reported medication adherence questionnaire

Patient adherence to their medications four weeks before hospitalization was assessed using a questionnaire that was developed, validated and used previously in similar studies (AbuRuz et al., 2006; Basheti et al., 2016a, 2016b) The questionnaire was composed of 8 items including the questions: how often did the patient forget to take his/her medication, stopped it from time to time, stopped it when feeling better, worse, or due to experiencing side-effects. The questionnaire was scored at a scale of 0 (never), 1 (rarely), 2 (sometimes), 3 (often) and 4 (always). Lower scores (score is out of 4) indicated better adherence. Patients were classified none-adherent (having inappropriate drug adherence) if they scored 1 or more in the total score (Morisky et al., 1986).

Patients reported reason that prevented them the most from taking their medication as prescribed. They were provided with options including high price; business (having no time); forgetfulness; medication dislike; ineffective medication; medication side effects; high number of medications.

2.8. Self-reported adherence to self-care activities questionnaire

Adherence to self-care activities was assessed using patient interview method. This validated questionnaire (AbuRuz et al., 2006) consisted of 5 questions assessing on how many days a week (7 days) did the patient follow a healthy diet at home (before hospitalization); eat 5 or more portions of fruit and/or vegetables; avoid eating food that contains high amount of fat (e.g. Full-fat milk and red meat); perform continuous exercise for more than 30 min; and perform special type of sports e.g. walking.

Patients diagnosed with diabetes mellitus were asked to answer three more questions: on how many days from the past one week did the patient check his/ her blood glucose, feet and shoes (Aburuz et al., 2011).

The total self-care score was calculated out of 35 (56 for diabetics). Higher scores indicated better adherence to self-care activities. Patients were then classified as none-adherent if they reported that they sometimes, usually or always ignored any of their recommended self-care activities (Aburuz et al., 2011).

2.9. Quality of life questionnaire

Stroke-specific health-related quality of life questionnaire (SS-QOL) was used in this study (Williams et al., 1999). This instrument is a valid, reliable, and responsive measure, for use in stroke clinical trials. It consists of 12 domains containing 49-item scale as follows- energy: 3 items, family roles: 3 items, language: 5 items, mobility: 6 items, mood: 5 items, personality: 3 items, self-care: 5 items, social roles: 5 items, thinking: 3 items, upper extremity function: 5 items, vision: 3 items, work/ productivity: 3 items. Based on the nature of each domain, each item was scored with the following key scoring: strongly agree: 1, moderately agree: 2, neither agree nor disagree: 3, moderately disagree: 4, strongly disagree: 5. Each patient had a score out of 245, the higher the score the better the quality of life.

2.10. The medication management review process

Following patient's interview, the clinical pharmacist (a pharmacist with masters in clinical pharmacy and a long standing experience in conducting the MMR service) screened each completed template and verified that all information in each patient template was correct and complete to be able to perform the medication management review successfully. Once the completion of the templates were approved, TRPs for each patient were assessed according to the following procedure: A classification system was

used by the researcher to identify the TRPs which either actually or potentially interfered with the clinical outcomes for each patient (AbuRuz et al., 2006). This system has been carefully explained and successfully applied in previous studies (Basheti et al., 2016a, 2013, 2017, 2016b) The system was used to identify unnecessary drug therapy, untreated condition/s, efficacy issues, safety issues, inappropriate knowledge, inappropriate adherence (to pharmacological therapy, self-care activities and/or none-pharmacological therapy) and miscellaneous problems. A systematic approach was utilized in identifying the TRPs (AbuRuz et al., 2006). Efficacy issues (more effective drug is available or recommended; the patient requires additional/combination therapy because of actual or potential therapy failure or because of guidelines recommendation) (AbuRuz et al., 2006) were identified through comparing patients' treatment with the most updated clinical practice evidence-based guideline recommendations. Appropriateness of dosing regimen was evaluated by comparing doses with recommendations from evidence-based guidelines or by using drug information references (Lexi-Comp, 2013). Actual adverse drug reactions were identified by conducting a review of the patient's reported symptoms and by investigating the patient's data for any possible adverse drug reactions related to their medications. Potential adverse drug reactions were also assessed and documented. The TRP severity was determined by the researcher (an experienced clinical pharmacist in this area) (Basheti et al., 2017; Basheti et al., 2016b; Dodd, 2003), and was classified accordingly into three different categories: minor TRP (one that if omitted would possibly have no influence on patient's results), moderate TRP (one that if the current practice is sustained could have an unwanted influence on patient's results), and major TRP (one that if the current practice is sustained could have a harmful influence on patient's results). All TRPs related to none-adherence and inappropriate knowledge were categorized as major. Inappropriate monitoring requirements were also categorized as major in most cases, especially when the last monitoring test was older than one year (Basheti et al., 2017; Basheti et al., 2016b; Dodd, 2003)

2.11. Sample size

To estimate the required sample size based on the primary outcome; which is the number of TRPs identified per patient, the result of a previous similar study conducted in Jordan was used (Basheti et al., 2013). With a standard deviation (SD) for the primary outcome of 2.80, and using the sample size equation $(1.96 * SD/\text{desired error})^2$, the minimum required sample size needed to estimate the average number of TRPs within an accuracy of 0.5 (desired error of 0.5) was found to be 120 patients. With a 20.0% drop out rate, it was planned to approach 144 patients for the study.

2.12. Data analysis

Upon evaluation of the submitted patients' data, findings for each patient were tabulated into the Statistical Package for Social Sciences (SPSS Inc. Cary, NC) version 21. To guarantee meeting all assumptions for the analysis used, preliminary data screening was done for all the study variables for normality, multicollinearity and proportional odd. The assumptions required for all statistical tests used were well met.

Being the most common conditions suffered by patients with stroke (McFarlane et al., 2005), the prevalence of hypertension and diabetes with the type and frequency of TRPs associated with the two medical conditions and their treatment were investigated.

The following TRPs were tabulated following identification: unnecessary drug therapy, untreated condition/s, ineffective/incomplete drug therapy, inappropriate dosage regimen, adverse drug effects, actual or potential drug interactions, none-adherence to none-pharmacological and pharmacological therapy, inappropriate patient knowledge, and suboptimal monitoring. TRP severity was tabulated according to the classification 'minor', 'moderate' and 'major'.

All categorical data were expressed as proportions (%), and continuous data as mean ± SD. Independent sample *t*-test was used for numerical data to identify significant differences among participants' responses. Univariate correlation analyses with Pearson correlation coefficient (r) was undertaken for the number of TRPs and SS-QOL scores.

In order to determine predictors of TRPs for stroke patients, a multiple linear regression analysis was performed. The dependent variable was the number of TRPs identified. Independent variables included age of patients, gender (females; males), marital status (single, married, divorced, widowed), place of living (urban; rural), patient education (illiterate, elementary, preparatory, secondary, diploma, bachelor degree, masters, doctor in philosophy), income (monthly income in Jordanian Dinar), smoking status (smoker, not smoker, ex-smoker), number of medical conditions, number of medications, and quality of Life score (out of 245).

As all data were classified using the validated classification system (Aburuz et al., 2011) by one researcher, it was not considered necessary to perform inter- or intra-rater variability analysis. For all analyses, statistical significance was established at $p < 0.05$.

3. Results

This study included 198 post-stroke patients During the study period, 198 eligible patients were recruited. None of the recruited patients refused to participate in the study (Fig. 1), and all of them completed the study (100% response rate).

3.1. Demographics and clinical characteristics

All of the study participants were hospitalized at the time of data collection. The mean age of participants was 56.62 ± 14.20, with 55.6% males. A great variation was reported with regard to patient educational level and work status. Only about a quarter of respondents reported to have a job (26.8%), the majority (78.0%) were married, lived with their own family (91.0%) and 53.4% lived in urban areas. Almost 70.0% of patients had hypertension and diabetes mellitus. Around 41.6% of patients were smokers. Regarding variation of time post-stroke, most patients (42.4%) developed the stroke within a month before entering the study, other within 6 months (34.3%). Many patients (31.4%) accepted to receive a follow-up home visit by a clinical pharmacist following discharge from the hospital to receive a medication management review service (Table 1).

The mean number of medications was (4.96 ± 2.34). The most frequent drug classes were anti-platelet, anti-hypertensive, anti-diabetic, and anti-hyperlipidemia medications. Among anti-hypertensive medications, an angiotensin-converting-enzyme inhibitor (ACEI, 25.8%), Beta Blocker (BB, 30.8%), and Calcium-Channel Blocker (CCB, 24.2%) were the most common drug classes (Table 2). The mean number of anti-hypertensive medications per patient was 2.00 ± 1.26, anti-diabetic 1.19 ± 0.70, anti-platelet 1.03 ± 0.26, and analgesics 1.06 ± 0.73.

3.2. Treatment related problems description

A total of 487 TRPs were identified during the study. The mean number of TRPs per patient was 2.45 ± 1.10. The most common TRP categories (Table 3) were efficacy (40.6%), inappropriate drug adherence (27.9%) and inappropriate knowledge (23.4%). Among

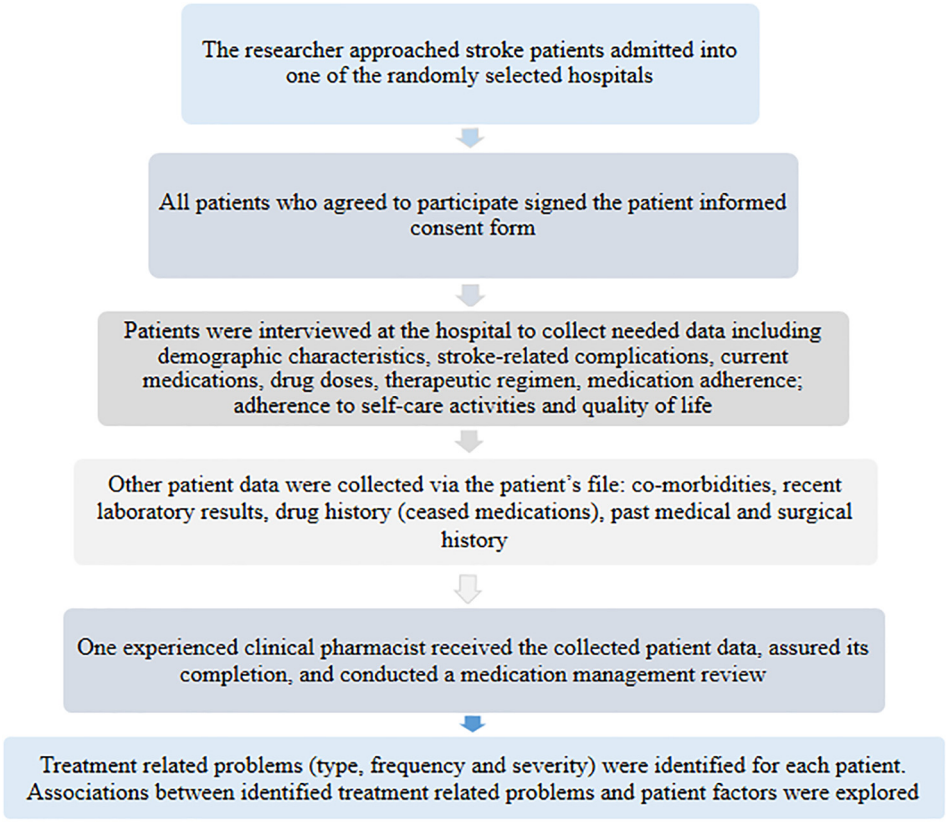

Fig. 1. Study procedure steps.

patients with hypertension and diabetes mellitus, efficacy and inappropriate drug adherence were the most common identified TRPs (Fig. 2). Of all the identified TRPs, more than 70.0% were of major severity. In particular, eighty-eight percent of the TRPs under the "efficacy" category were major in severity, 99.3% of TRPs were major in severity under the "inappropriate drug adherence" category. Table 4 shows the types and frequencies of TRPs according to clinical significance. As mentioned above, drug efficacy was one of the most commonly identified TRPs. An example of this category is the patient who has both diabetes mellitus and hypertension and is not using ACEI or Angiotensin Receptor Blockers (ARBs) as recommended by updated therapeutic guidelines. Most of the patients were none-adherent to their medications because they forgot or skipped the dose, such a case can be classified under "Inappropriate drug adherence" category. More examples are shown in Table 5 (see Fig. 3.).

3.3. Medication adherence

The mean adherence score was found to be 1.81 (0.61) with a range of 0.0 to 3.5. Results showed that a minority of patients (10.7% to 33%) never stopped their medication due to any of the discussed reasons (Table 6). About half of the patients (53.3%) reported to never/rarely forget to take their medication, 56.3% never/rarely stop their medication from time to time; 54.2% never/rarely stop their medication when they feel better; 52.8% never/rarely stop their medication when they feel worse after taking their medications. Only one third of the patients (36.6%) never/rarely stop their medication due to side effects they suffer from it.

Patients reported that high number of medications (30.2%) followed by forgetfulness (29.3%) are the two main reasons that often/always prevented them from taking their medications as prescribed, leading to none-adherence.

As for adherence to the clinical pharmacist advice, only 26.6% of the patients reported that they often/always did that.

3.4. Self- care activity

The mean self-care score (out of 35) was low, equaling to 0.30 (4.69; range of 1 to 31); similar results were reported for patients with diabetes (score = 18.30 (7.64; range of 1 to 34; score out of 56). About a quarter of the respondents reported that they were on diet and eat 5 or more of vegetables and fruits' shares a week (Table 7). Around 60.0% of the patients did not exercise or perform any special type of sports (e.g. walking).

For diabetic patients, 37.5% did not measure their blood glucose at all, or check their feet (38%) and about half of the patients (51.9%) never checked their shoes. All of the patients were classified as none-adherent to self-care activities, as they all reported to 'sometimes', 'usually' or 'always' ignore performing it (Table 7).

3.5. Quality of life scores

Patients had a mean SS-QOL score of 137.21 (39.73), ranging between 86.00 and 228.00. No significant difference between genders was found (males 139.91 (41.89) vs. females 134.30 (36.92), $p = 0.328$). Significant correlation between the number of TRPs and SS-QOL scores was found, indicating the less the TRPs the better the patient's quality of life ($r = -0.263$; $p < 0.001$).

Patients who agreed to receive the follow-up home visit from the pharmacist had a significantly lower SS-QOL score than those who refused 124.63 (41.75) vs. 145.05 (42.36), $p = 0.006$.

Table 1
Demographics and clinical characteristics of the study population (n = 198).

Characteristics	Frequency	%
Age (M = 56.6, SD = 14.2)		
Income (M = 502 JD, SD = 192.2)		
Sufficient	90	45.5
Not sufficient	108	54.5
Gender		
Males	110	55.6
Females	88	44.4
Education		
Elementary	49	24.9
Preparatory	40	20.3
Secondary	40	20.3
Diploma	25	12.7
BSc	27	13.7
MSc &PhD	16	8.1
Job		
Work	53	26.8
Don't work	95	48.0
Retired	50	25.3
Marital status		
Single	17	8.6
Married	155	78.3
Divorce or Widow	26	13.1
Lives with		
No body (alone)	15	7.6
My family	180	90.9
My spouse family	3	1.5
Place of living		
Urban	103	53.4
Rural	90	46.6
Smoking status		
Smoker	82	41.6
None-smoker	102	51.8
Ex-smoker	11	5.6
When you get the stroke		
Less than a month	84	42.4
A month to <2 months	41	20.7
2 months to 6 months	27	13.6
More than 6 months	31	15.7
Other chronic conditions		
None	61	30.8
Diabetes	11	5.6
Hypertension	47	23.7
Diabetes and hypertension	79	39.9
Accept Home visit for MMR*		
Yes	49	31.4
No	107	68.6

* MMR: Medication Management Review.

Table 2
Most frequent drug classes used by the study sample (n = 198).

Most frequent drug classes, n (%)	
Anti-hypertensive	
ACEI	51 (25.8)
ARBs	17 (8.6)
BB	61 (30.8)
CCB	48 (24.2)
Diuretics	36 (18.2)
Vasodilators	11 (5.8)
Anti-diabetic	
OADA	48 (24.2)
Insulin	34 (17.2)
Anti-hyperlipidemia	92 (46.5)
Anti-platelet	176 (88.9)
PPI	66 (33.3)
H_2B	34 (17.2)
Analgesic	83 (41.9)
Most frequent drug classes, mean (SD)	
Number of drugs per patient	4.96 (2.338)
Anti-hypertensive	2 (1.26)
Anti-diabetic	1.19 (0.70)
Anti-platelet	1.03 (0.26)
Anti-hyperlipidemia	0.82 (0.38)
Gastrointestinal drugs	0.92 (0.40)
Analgesics	1.06 (0.727)

ACEI: An angiotensin-converting-enzyme inhibitor.
ARBs: Angiotensin II receptor blockers.
BB: Beta Blocker.
CCB: Calcium Channel Blocker.
OADA: Oral Anti-Diabetic Agent.
PPI: Proton Pump Inhibitors.
H_2B: H_2 Blocker.

3.6. Association between patient factors and TRPs for stroke patients

Multiple linear regression modelling numbers of TRPs indicated that gender, patient education, smoking status, number of drugs and SS-QOL score were the variables significantly associated with higher TRP numbers ($R^2 = 0.318$, $p < 0.001$, Table 8); while age, marital status, place of living, income and number of medical conditions were not significant factors. Higher number of identified TRPs was associated with being a male, having a lower educational level, being a current smoker, having a higher number of medications and a poorer quality of life.

4. Discussion

Up to authors' knowledge, this study is the first to apply the MMR service with the aim to identify the type, frequency and severity of TRPs for post-stroke patients admitted into hospital, shedding light on patient factors associated with the TRPs. The study established that the most common categories of TRPs were lack of drug efficacy (40.6%), inappropriate drug adherence (27.9%) and inappropriate patient knowledge (23.4%), with more than 70.0% of the TRPs categorized as 'major' in severity. A significant association between higher number of TRPs and being a male, a current smoker, having lower educational level, higher number of medications and poorer quality of life was shown. Identifying TRPs for post-stroke patients and the associated patient factors can help in planning strategies aimed at decreasing the incidence of stroke.

Tobacco use is among the most significant modifiable risk factors in patients with stroke (World Health Organization, 2018). Among those aged under 65, two-fifths of deaths from stroke are linked to smoking (World Health Organization, 2018). The incidence of stroke is declining in many developed countries, largely as a result of better control of high blood pressure and reduced levels of smoking. However, in Jordan, smoking (cigarettes smoking and waterpipe smoking) still presents a major health concern amongst the young and educated males and females (Sweis and Chaloupka, 2014). Jordan, a developing country with one of the smallest economies in the Middle East has a 55.9% prevalence of smoking among males, versus 23.7% among females (Sweis and Chaloupka, 2014). This study has shown that 48% of the patients were smokers or ex-smokers. Educational programs and effective policies are needed to combat smoking in the country, keeping in mind that differences between genders exist and that one policy might not fit all (Sweis and Chaloupka, 2014).

Important TRPs were identified in this study, matching previous findings, with drug efficacy problems being one of the highest TRP categories identified (Celin and Ramesh, 2012). In an Australian study looking into TRPs in 1000 patients living in the community, the miscellaneous (need for laboratory test) was found to be the most frequent TRP category identified among stroke patients (33.0%) (Roughead et al., 2004). A study conducted in Northern Sweden looking into the occurrence and character of TRPs among old patients with dementia or cognitive impairment, found that ineffective drug/inappropriate drug (efficacy problem category) and unnecessary drug therapy were the most common TRPs among

Table 3
Prevalence and type of treatment related problems (TRPs) in the study population (n = 198).

Treatment related problems (TRPs)	Frequency of TRP, n (%)
1. Unnecessary drug therapy	**10 (2.1%)**
1.a Drug use without an indication	1 (0.2%)
1.b Addiction or recreational drug use	0 (0.0%)
1.c The patient treatment should be stepped down	0 (0.0%)
1.d Duplication	9 (1.9%)
1.e Treating avoidable adverse reaction	0 (0.0%)
2. Untreated conditions	**17 (3.5%)**
3. Efficacy	**198 (40.6%)**
3.a More effective drug is available/recommended	23 (4.7%)
3.b The patient requires additional/combination therapy	118 (24.2%)
3.c Efficacy dosage regimen issue	57 (11.7%)
3.d Efficacy interaction issue	1 (0.2%)
4. Safety	**7 (1.4%)**
4.a A current drug is contraindicated/unsafe	1 (0.2%)
4.b Safer drug is recommended	0 (0.0%)
4.c High risk for ADR	1 (0.2%)
4.d Allergic reaction or undesirable effect	3 (0.6%)
4.e Safety dosage regimen issue	1 (0.2%)
4.f Safety interaction issue	1 (0.2%)
5. Inappropriate knowledge	**114 (23.4%)**
5.a The patient is not instructed or does not understand important information regarding his medication	17 (3.5%)
5.b The patient is not instructed or does not understand important information regarding none-pharmacological therapy	97 (19.9%)
6. Inappropriate adherence	**136 (27.9%)**
6.a Problem in adherence to pharmacological therapy	135 (27.7%)
6.b Drug is not available	1 (0.2%)
6.c Problem in adherence to self-care activities or none-pharmacological therapy	0 (0.0%)
7. Miscellaneous	**4 (0.8%)**
7.a A need for additional or more frequent monitoring	4 (0.8%)
7.b A need for additional diagnostic test	0 (0.0%)
7.c A need for consultation	0 (0.0%)
7.d The chosen drug is not cost effective	0 (0.0%)
7.e Other dosage regimen issues	0 (0.0%)
7.f Other interaction issue	0 (0.0%)
7.g Administering errors	0 (0.0%)
7.h Dispensing errors	0 (0.0%)

Percentage is within the total number of treatment related problems (487 problems).

Table 4
Prevalence and type of treatment related problems (TRPs) according to clinical significance.

TRP	Clinical Significance, n (%)*
Unnecessary drug therapy	Major 10 (100) Moderate 0 (0.0) Minor 0 (0.0)
Untreated condition	Major 17 (100) Moderate 0 (0.0) Minor 0 (0.0)
Efficacy	Major 175 (88.3) Moderate 24 (12.1) Minor 0 (0.0)
Safety	Major 5 (71.4) Moderate 2 (28.6) Minor 0 (0.0)
Inappropriate knowledge	Major 17 (14.9) Moderate 97 (85.0) Minor 0 (0.0)
Inappropriate adherence	Major 135 (99.3) Moderate 1 (0.7) Minor 0 (0.0)
Miscellaneous	Major 0 (0.0) Moderate 4 (100) Minor 0 (0.0)
All treatment related problems	Major 359 (73.1) Moderate 128 (26.3) Minor 0 (0.0)
Mean number of TRPs per patient (SD)	2.45 (1.101)

* n (%) within each category of treatment related problems.

patients with an earlier stroke (Pfister et al., 2017). In India, 120/133 patients with stroke were found to have at least one TRPs, and drug efficacy problem was found to be the highest among the TRPs identified, accounting for 35.0% (Kanagala et al., 2016). In a study conducted in Germany, TRPs occurred in 105/155 (67.7%) patients with transient ischemic attack or ischemic stroke, giving a mean of 1.80 ± 2.00 TRPs per patient; inappropriate "drug" therapy, "indication", and "dosage" were the most common TRPs identified (Hohmann et al., 2012). Dissimilarities between the studies from different countries were found, explained probably by the dif-

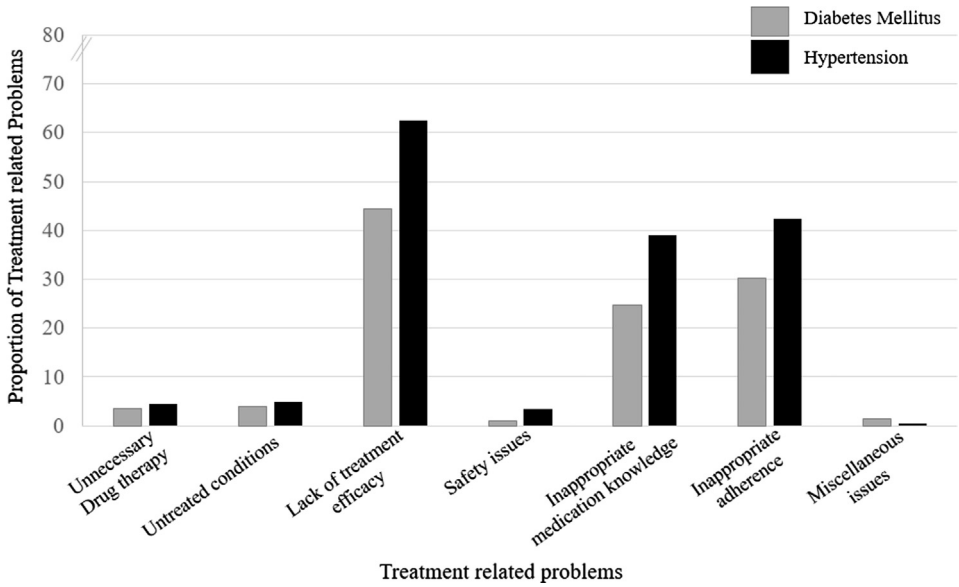

Fig. 2. Treatment related problems (TRPs) associated with the most prevalent chronic medical conditions for study participants (n = 198).

Table 5
Examples on the type of treatment related problems (TRPs) for the most frequent chronic medical conditions and drug classes identified in this study.

TRP category	Example
Unnecessary drug therapy	
Duplication	A patient was on two therapies from different classes i.e. Ranitidine & Omeprazole for the same indication as gastrointestinal prophylaxis
Untreated condition	
An untreated Condition	Diabetic patient with stroke and hypertension with no secondary prevention therapy i.e. aspirin and atorvastatin or other statins Pre-diabetic patient required therapy such as metformin (Glucophage®) 500 mg TID
Ineffective/incomplete drug therapy	
More effective drug is available/recommended	Hypertensive diabetic patient should be on more effective therapy (ACEI or ARBs) if not contraindicated instead of BB or CCB
Efficacy dose regimen issue	Anemic patient on twice daily dosing of ferrous gluconate where the appropriate dose is 300 mg 2 × 3
Safety	
Allergic reaction or undesirable effect	Elderly patient with stroke and hypertension is on a high dose of warfarin (10 mg daily) with bruises on his arms and incidents of bleeding
Inappropriate knowledge	
The patient is not instructed or does not understand important information regarding his medication	Hypertensive diabetic patient does not understand the importance of taking his medication (ACEI) on daily basis.
The patient is not instructed or does not understand important information regarding none-pharmacological therapy	The patient is not instructed about self-care advice such as on smoking, alcohol, diet or exercise
Inappropriate adherence	
Problem in adherence to medication	Elderly patient with stroke and hypertension is none-adherent to his medications because of their high number and because of forgetting to take all of them
Miscellaneous	
A need for additional or more frequent monitoring	Elderly patient with stroke and hypertension has no monitoring of lipid profile for the previous 2 years

ACEI: Angiotensin Converting Enzyme Inhibitors; ARBs: Angiotensin Receptor Blockers; BB: Beta Blockers; CCB: Calcium Channel Blockers.

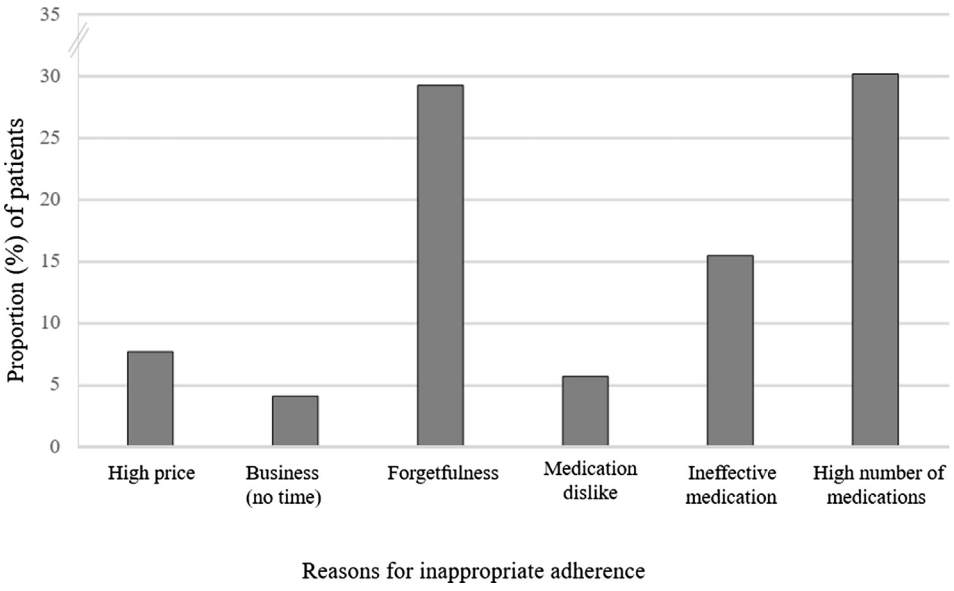

Fig. 3. Proportion of stroke patients (n = 198) reported reasons for lack of adherence to their medications.

ference in patients' lifestyle, prevalence of chronic conditions, and the healthcare system provided to the patients. Identified TRPs for patients with stroke were mostly categorized as 'major' in severity; a fact identified in this study and previously (70% vs. 83%) (Celin and Ramesh, 2012).

The World Health Organization identified the issue of adherence to medications as a growing concern adding to the burden of disease (World Health Organization, 2003). In this study, "inappropriate drug adherence" was found to be one of the most common TRPs affecting stroke patients. Many of the participants who had hypertension (42.4%) and diabetes mellitus (30.3%) were found to be none-adherent to their medications. Medication none-adherence for stroke patients has been associated with increased comorbidity (Kronish et al., 2013). This finding was expected, as Ireland et al found that<51.0% of stroke patients were adherent to their medications (Ireland et al., 2010), while Kronish et al showed that 40.0% had poor self-reported medication adherence (Kronish et al., 2013). This issue is vital considering that the risk of recurrent stroke gets reduced by up to 38.0% when patients were adherent to their antiplatelet therapy (Fan et al., 2010). Further-

Table 6
Patient self-reported medication adherence (n = 198).

Question, n (%)	Never (0)	Rarely* (1)	Sometimes* (2)	Often* (3)	Always (4)
1. Do you forget to take your medication?	65 (33.0)	40 (20.3)	62 (31.5)	23 (11.7)	7 (3.6)
2. Do you stop your medication from time to time?	68 (34.5)	43 (21.8)	57 (28.9)	18 (0.1)	11 (5.6)
3. Do you stop your medication when you feel better?	62 (32.0)	43 (22.2)	49 (25.3)	24 (12.4)	16 (8.2)
4. Do you stop your medication when you feel worse after taking your medication?	33 (16.9)	70 (35.9)	46 (23.6)	20 (10.3)	26 (13.3)
5. Do you stop your medication due to a side affect you believe is due to taking your medication?	21 (10.7)	51 (25.9)	57 (28.9)	34 (17.3)	34 (17.3)
6. Do you fail to follow your clinical pharmacist advice?	28 (14.3)	46 (23.5)	70 (35.7)	25 (12.8)	27 (13.8)
7. How often a week you do not take your medication (you forget or stop)?	47 (24.4)	28 (14.5)	69 (35.8)	20 (8.9)	8 (4.1)
8. The following reason/s prevent/s you the most from taking your medication/s:					
High price	169 (87.1)	8 (4.1)	2 (1.0)	3 (1.5)	12 (6.2)
Business (no time)	175 (90.7)	8 (4.1)	2 (1.0)	0 (0.0)	8 (4.1)
Forgetfulness	105 (55.0)	19 (9.9)	11 (5.8)	4 (2.1)	52 (27.2)
Medication dislike	152 (78.4)	3 (1.5)	3 (1.5)	2 (1.0)	34 (17.5)
Ineffective medication	178 (92.7)	1 (0.5)	2 (1.0)	0 (0.0)	11 (5.7)
Medication side effects	151 (78.2)	7 (3.6)	5 (2.6)	2 (1.0)	28 (14.5)
High number of medications	125 (65.1)	4 (2.1)	5 (2.6)	3 (1.6)	55 (28.6)

* Rarely: less than one dose every week; sometimes: one dose a week; often: two doses a week; always: more than two doses a week. Score out of 4 for each patient, with the lower the score the better the adherence. Patients were considered under-adherent if they scored 1 or more in the total score.

Table 7
Assessment of self-care activities for study population (n = 198).

Statement, n (%)	None	Once	Twice	Three times	Four times	Five & more
1. On how many days a week did you follow a healthy diet	57 (29.2)	11 (5.6)	19 (9.7)	25 (12.8)	29 (14.9)	54 (27.6)
2. On how many days a week did you eat 5 or more #portions of vegetables and/or fruits	33 (16.8)	26 (13.3)	28 (14.3)	26 (13.3)	29 (14.8)	54 (27.5)
3. On how many days a week did you skip eating food that contains high amount of fat (e.g. Full-fat milk and red meat)	18 (9.2)	44 (22.4)	53 (27.0)	19 (9.7)	36 (18.4)	26 (13.3)
4. On how many days a week did you perform continuous exercise for more than 30 min	118 (60.2)	39 (19.9)	17 (8.7)	11 (5.6)	4 (2.0)	7 (3.5)
5. On how many a week did you perform special type of sport e.g. walking	123 (63.1)	22 (11.3)	28 (14.4)	15 (7.7)	4 (2.1)	3 (1.5)
Mean self-care score * (mean, SD)	10.30 (4.69); range (1–31)					
6. On how many days a week did you measure your blood glucose level	72 (37.5)	42 (21.9)	19 (9.9)	19 (9.9)	13 (6.8)	27 (14.1)
7. On how many days a week did you check your feet	30 (38.0)	8 (10.1)	7 (8.9)	14 (17.7)	6 (7.6)	14 (17.7)
8. On how many days a week did you checked your shoes	41 (51.9)	5 (6.3)	7 (8.9)	8 (10.1)	8 (10.1)	10 (12.7)
Mean self-care score for patients with diabetes (mean, SD)	18.30 (7.64); range (1–34)					

* The total self-care score is out of 35 (56 for diabetics). All patients answered questions 1–6; only diabetic patients answered questions 6, 7 and 8. Higher scores indicated better self-care adherence.
# Each portion equals to one piece of fruit/vegetable.

more, stroke is uncommon in people under 40 years, but when it does occur, the main cause is high blood pressure (World Health Organization, 2018). None-adherence to antihypertensive medications have a major role as a cause, as for every 10 people who die of a stroke, four could have been saved if their blood pressure had been regulated (World Health Organization, 2018). The case is similar for hospitalized patients for acute stroke and history of hypertension, a significant association between the incidence of stroke and not taking the medications as prescribed has been documented (Baune et al., 2004). Conclusively, adherence to medications is a crucial part of patient care and crucial for reaching clinical aims, and pharmacists have a significant role in this area (Basheti et al., 2016a).

The highest proportion of chronic conditions reported among the current study sample was hypertension and diabetes, which is expected and consistent with previous studies (Ayasrah et al., 2018; Basheti et al., 2016a; Basheti et al., 2013) The most frequently used drug classes in this study were anti-platelets, anti-hypertensive, anti-diabetic, and anti-hyperlipidemia medications, also consistent with other studies, reporting anti-hypertensive and anti-diabetic agents as the most frequent drug classes used by chronically ill patients (Basheti et al., 2016a). Such medications accounted for the majority of the identified TRPs. Cardiovascular and nervous system medicines were shown to be the most common implicated medications previously, accounting for 69.0% of the medication-related problems for patients with stroke (Roughead et al., 2004). Majority of patients in the current study (88.9%) were found to use antiplatelet therapy. Although patients on such medications were shown previously to have significant reduction in stroke risk (Silva-Smith, 1994), such critical medications require continuous education by the pharmacist to prevent potential complications and drug interactions (Silva-Smith, 1994).

Pharmaceutical care services have demonstrated significant improvements in patient care, including adherence to treatment resulting in significant (41.0%) reduction in mortality over 2 years (Wu et al., 2006), better control of chronic conditions and reduced overall healthcare costs (Bernsten et al., 2001). Such services have been shown to improve patient outcomes for diabetes, hypertension, anticoagulation, and other chronic diseases including stroke (Basheti et al., 2016a; Chiquette et al., 1998; Chisholm-Burns et al., 2010). Significantly more hospitalized stroke patients who received an MMR by a pharmacist were found to be on antihypertensive and antithrombotic agents compared to patients not reviewed previously by the pharmacist (Khalil et al., 2015). A study conducted by McAlister and colleagues has assessed pharmacist-managed drug therapy for dyslipidemia and hypertension in patients with a recent ischemic stroke or tertiary ischemic attacks; within this study, patients in the pharmacist-managed group were

Table 8
Summary of the regression model obtained for the dependent variable, number of treatment related problems (n = 172).

Variable	Beta	t	P value
Age of patients	0.062	0.906	0.366
Gender	0.168	2.284	**0.024**
Marital status	0.062	0.883	0.378
Place of living (urban vs. rural)	−0.012	−0.176	0.860
Patient education	−0.222	−2.502	**0.013**
Income[†]	−0.133	−1.639	0.103
Smoking status	−0.236	−3.078	**0.002**
Medical conditions	0.124	1.852	0.066
Number of drugs	0.186	2.573	**0.011**
[#]Quality of Life score	−0.191	−2.791	**0.006**

This table shows the output from a multivariable regression analysis in which total number of treatment related problems (TRPs) was the dependent variable. "Beta" is the standardized regression coefficient. The overall fit of the model was $R^2 = 0.318$, $P < 0.001$.

[†] Income (monthly income in Jordanian Dinar; 0.71JD = 1USD).

[#] Quality of life score (score out of 245, the higher the score the better the quality of life). Numbers in **'bold'** indicate significant results.

more likely to get goal blood pressure and lipid values at six-month interval than patients in the nurse-managed group (McAlister et al., 2014). Consistent with these findings, Cording et al found that 77.0% of patients with stroke achieved their low-density lipoprotein (LDL) goal after pharmacist involvement in lipid clinic, compared to 44.0% at baseline (Cording et al., 2002). Generally speaking, the evidence for pharmacist participation in dyslipidemia and hypertension management is significant, hence, the impact that pharmacists can have on modifiable risk factors for stroke patients can be substantial resulting in reduction in rates of recurrent stroke (Lindblad & Howorko, 2008; Sookaneknun et al., 2004).

Patient's quality of life can also be improved through these services; a study conducted in Germany demonstrated the potential impact of intensified pharmaceutical care for patients with ischemic stroke on quality of life (Hohmann et al., 2010). In this study, a higher number of TRPs was associated with a poorer quality of life, two factors that can be improved through the MMR service. In addition, patients who agreed to receive the follow-up home visit from the clinical pharmacist showed a lower quality of life score than those who refused. This may possibly indicate higher patient need of close care. This is not surprising, considering that pharmaceutical care services, including medication management reviews, have shown previously to stabilize quality of life score for patients with stroke who were discharged home in contrast to patients who did not receive the service and ending with a worsened quality of life score (Hohmann et al., 2009). Hence, outcomes of this study call onto the policy makers in Jordan and other similar developing countries to pave the way towards the active involvement of pharmacists in the continuous management of patients with stroke, via initiating services such as the MMR service (Lindblad & Howorko, 2008).

Study strength includes presenting results that reflect the situation in all of the socio-demographic sectors of Jordan, increasing the generalizability of the findings reported. Nine major hospitals representing the three major health sectors in Jordan, including military, governmental, and educational hospitals (university teaching hospitals) were involved. A validated TRPs classification system was used (AbuRuz et al., 2006), which has been carefully explained and successfully applied in previous studies (Ayasrah et al., 2018; Basheti et al., 2016a, 2013). An experienced clinical pharmacist who possesses a strong background in the area of clinical pharmacy, pharmacotherapy and pharmaceutical care conducted the reviews for all study patients.

The study comes with few limitations. The time after which patient data was collected post-stroke may have impacted the frequency, type, and/or severity of TRPs identified. Assessment of patient adherence to their medications and self-care activities were based on their recall of what they did at home before hospital admission, which may lack accuracy due to forgetfulness. The proportions of self-medication and use of alternative and complementary medicines were not verified, knowing that in Jordan, many chronically ill patients use herbal remedies that can interact with their treatments (Issa & Basheti, 2016). Private hospitals were not included in this study, which can be beneficial for future research considering the widespread of private hospitals in Jordan. The face-to-face interviews conducted to collect patient data were completed by trained research nurses for feasibility purposes; it would be preferable for future studies to have the clinical pharmacist perform the face-to-face interviews. Being the most common chronic conditions suffered by stroke patients, hypertension and diabetes were explored in this study; future research should explore other chronic conditions. Type of stroke was not investigated in this study as different types may be associated with different outcomes (World Health Organization, 2018). According to the adherence assessment tool used, patients were classified as none-adherent if they scored one or more in the total score. This meant that a patient can answer "rarely" to one of the questions, and be considered as none-adherent, presenting a thin border of assessment.

5. Conclusion

Patients with stroke suffer a high number of TRPs, most of which are major in severity. This sheds light on the importance of the role of the pharmacist in providing the MMR service for post-stroke patients in Jordan and aboard. The most common categories of TRPs identified were lack of drug efficacy, inappropriate drug adherence and inappropriate patient knowledge. Higher number of TRPs were significantly associated with being a male, a current smoker, having lower educational level, higher number of medications and poorer quality of life. Future studies should investigate the value of the MMR service in improving post-stroke patients' use of their treatment and their quality of life, taking into account the present identified factors associated with patient treatment. Considering the findings of this study when planning individualized patient care plans and future pharmaceutical services for post-stroke patients can be worthwhile.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgments

The authors are grateful to the Applied Science Private University Amman, Jordan, for the full financial support granted to this research project. The authors wish to thank the healthcare professionals and patients who participated in this study, and Dr. Mohammad Basheti for his valuable contribution.

Funding

The authors are grateful to the Applied Science Private University, Amman, Jordan, for the financial support granted to this research project.

Conflict-of-interest

No financial or other potential conflicts of interest exist.

Contribution

All Authors have similar contribution to all parts of this study.

References

Aburuz, S., Al-Ghazawi, M., Snyder, A., 2012. Pharmaceutical care in a community-based practice setting in Jordan: where are we now with our attitudes and perceived barriers? Int. J. Pharm.Pract 20, 71–79. https://doi.org/10.1111/j.2042-7174.2011.00164.

AbuRuz, S.M., Bulatova, N.R., Yousef, A.M., 2006. Validation of a comprehensive classification tool for treatment-related problems. Pharm. World Sci. 28, 222–232. https://doi.org/10.1007/s11096-006-9048-0.

Aburuz, S.M., Bulatova, N.R., Yousef, A.M., Al-Ghazawi, M.A., Alawwa, I.A., Al-Saleh, A., 2011. Comprehensive assessment of treatment related problems in hospitalized medicine patients in Jordan. Int. J. Clin. Pharm. 33, 501–511. https://doi.org/10.1007/s11096-011-9497-y.

Al Alawneh, M., Nuaimi, N., Basheti, I.A., 2018. Pharmacists in humanitarian crisis settings: assessing the impact of pharmacist-delivered home medication management review service to Syrian refugees in Jordan. Res. Social. Adm. Pharm. 10, 30858–130856.

Altowaijri, A., Phillips, C.J., Fitzsimmons, D., 2013. A systematic review of the clinical and economic effectiveness of clinical pharmacist intervention in secondary prevention of cardiovascular disease. J. Manag. Care Pharm. 19, 408–416. 410.18553/jmcp.12013.18519.18555.18408.

Arowoiya, A.I., Elloker, T., Karachi, F., Mlenzana, N., Khuabi, L.J., Rhoda, A., 2017. Using the World Health Organization's Disability Assessment Schedule (2) to assess disability in community-dwelling stroke patients. S. Afr. J. Physiother. 73 (343), 2017. 310.4102/sajp.v4173i4101.4343.eCollection.

Australian Government Medicare Australia, Department of human services. Residential Medication Management Review. (Available online at: http://www.medicareaustralia.gov.au/provider/pbs/fifth-agreement/residential-medication-management-review.jsp. Accessed June 2018).

Ayasrah, S.M., Ahmad, M.M., Basheti, I.A., 2018. Post-stroke depression in Jordan: prevalence correlates and predictors. J. Stroke Cerebro Vas Dis. 27, 1134–1142. 10.1016/j.jstrokecerebrovasdis.2017.11.027.

Bader, L.R., McGrath, S., Rouse, M.J., Anderson, C., 2017. A conceptual framework toward identifying and analyzing challenges to the advancement of pharmacy. Res. Social. Adm. Pharm. 13, 321–331. 310.1016/j.sapharm.2016.1003.1001.

Barnett, K., Mercer, S.W., Norbury, M., Watt, G., Wyke, S., Guthrie, B., 2012. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 380, 37–43. https://doi.org/10.1016/S0140-6736(1012)60240-60242.

Basheti, I.A., Al-Qudah, R.A., Obeidat, N.M., Bulatova, N.R., 2016a. Home medication management review in outpatients with chronic diseases in Jordan: a randomized control trial. Int. J. Clin. Pharm. 38, 404–413. https://doi.org/10.1007/s11096-016-0266-9.

Basheti, I.A., Qunaibi, E.A., Bulatova, N.R., Samara, S., AbuRuz, S., 2013. Treatment related problems for outpatients with chronic diseases in Jordan: the value of home medication reviews. Int. J. Clin. Pharm. 35, 92–100.

Basheti, I.A., Qunaibi, E.A., Hamadi, S.A., Abu-Gharbieh, E., Saleh, S., AbuRuz, S., Mohamoud, M., Bulatova, N.R., 2014. Patient perspectives of the role of the community pharmacist in the Middle East: Jordan, United Arab Emirates and Iraq. Pharmacol Pharm 5, 588–599.

Basheti, I.A., Rizik, M., Bulatova, N.R., 2017. Home medication management review in outpatients with alarming health issues in Jordan: a randomized control trial. J. Pharm. Health Serv. Res. https://doi.org/10.1111/jphs.12213.

Basheti, I.A., Tadros, O.K., Aburuz, S., 2016b. Value of a community-based medication management review service in Jordan: a prospective randomized controlled study. Pharmacotherapy 36, 1075–1086. https://doi.org/10.1002/phar.1833.

Basheti, I.A., Tadros, O.K., Alnajjar, M.S., Aburuz, S., 2018. Assessing patient satisfaction with the Medication Management Review Service delivered in Jordan. J. Pharm. Health Serv. Res. 10.1111/jphs.12233.

Baune, B.T., Aljeesh, Y.I., Bender, R., 2004. The impact of non-compliance with the therapeutic regimen on the development of stroke among hypertensive men and women in Gaza, Palestine. Saudi Med. J. 25, 1683–1688.

Bernsten, C., Bjorkman, I., Caramona, M., Crealey, G., Frokjaer, B., Grundberger, E., Gustafsson, T., Henman, M., Herborg, H., Hughes, C., McElnay, J., Magner, M., van Mil, F., Schaeffer, M., Silva, S., Sondergaard, B., Sturgess, I., Tromp, D., Vivero, L., Winterstein, A., 2001. Improving the well-being of elderly patients via community pharmacy-based provision of pharmaceutical care: a multicentre study in seven European countries. Drugs Aging 18, 63–77.

Celin, A.T., Seuma, J., Ramesh, A., 2012. Assessment of drug related problems in stroke patients admitted to a south indian tertiary care teaching hospital. Ind. J. Pharm. Prac. 5, 28–33.

Chiquette, E., Amato, M.G., Bussey, H.I., 1998. Comparison of an anticoagulation clinic with usual medical care: anticoagulation control, patient outcomes, and health care costs. Arch. Intern. Med. 158, 1641–1647.

Chisholm-Burns, M.A., Kim Lee, J., Spivey, C.A., Slack, M., Herrier, R.N., Hall-Lipsy, E., Graff Zivin, J., Abraham, I., Palmer, J., Martin, J.R., Kramer, S.S., Wunz, T., 2010. US pharmacists' effect as team members on patient care: systematic review and meta-analyses. Med. Care 48, 923–933. 910.1097/MLR.1090b1013e3181e57962.

Christensen, M., Lundh, A., 2013. Medication review in hospitalised patients to reduce morbidity and mortality. Cochrane Database Syst. Rev. 2, CD008986.

Cording, M.A., Engelbrecht-Zadvorny, E.B., Pettit, B.J., Eastham, J.H., Sandoval, R., 2002. Development of a pharmacist-managed lipid clinic. Ann. Pharmacother. 36, 892–904. 10.1345/aph.1A158.

de Freitas, G.R.M., Neyeloff, J.L., Balbinotto Neto, G., Heineck, I., 2018. Drug-related morbidity in Brazil: a cost-of-illness model. Value Health Reg Issues 17, 150–157. https://doi.org/10.1016/j.vhri.2018.1007.1002.

Dodd, C., 2003. Assessing pharmacy interventions at Salisbury Health Care NHS Trust. Hosp. Pharm. 10, 451–456.

Ehntholt, K.A., Yule, W., 2006. Practitioner review: assessment and treatment of refugee children and adolescents who have experienced war-related trauma. J. Child Psychol. Psychiatry 47, 1197–1210. JCPP1638. [pii] 10.1111/j.1469-7610.2006.01638.

Elayeh, E., Akour, A., Almadaeen, S., AlQhewii, T., Basheti, I.A., 2017. Practice of pharmaceutical care in community pharmacies in Jordan. Trop. J. Pharm. Res. 16, 463–470.

Fan, J.C., Mysak, T.M., Jeerakathil, T.J., Pearson, G.J., 2010. Secondary stroke prevention: practice patterns in a tertiary care stroke service. Can. J. Neurol. Sci. 37, 245–251.

Gallacher, K.I., Batty, G.D., McLean, G., Mercer, S.W., Guthrie, B., May, C.R., Langhorne, P., Mair, F.S., 2014. Stroke, multimorbidity and polypharmacy in a nationally representative sample of 1,424,378 patients in Scotland: implications for treatment burden. BMC Med. 12, 151. https://doi.org/10.1186/s12916-12014-10151-12910.

Hackett, M., Anderson, C., 2005. Treatment options for post-stroke depression in the elderly. Aging Health 1, 95–105.

Hohmann, C., Klotz, J.M., Radziwill, R., Jacobs, A.H., Kissel, T., 2009. Pharmaceutical care for patients with ischemic stroke: improving the patients quality of life. Pharm. World Sci. 31, 550–558. 510.1007/s11096-11009-19315-y.

Hohmann, C., Neumann-Haefelin, T., Klotz, J.M., Freidank, A., Radziwill, R., 2012. Drug-related problems in patients with ischemic stroke in hospital. Int. J. Clin. Pharm. 34, 828–831. 810.1007/s11096-11012-19690-11097.

Hohmann, C., Radziwill, R., Klotz, J.M., Jacobs, A.H., 2010. Health-related quality of life after ischemic stroke: the impact of pharmaceutical interventions on drug therapy (pharmaceutical care concept). Health Qual Life Outcomes 8, 59. https://doi.org/10.1186/1477-7525-1188-1159.

Ireland, S., MacKenzie, G., Gould, L., Dassinger, D., Koper, A., LeBlanc, K., 2010. Nurse case management to improve risk reduction outcomes in a stroke prevention clinic. Can. J. Neurosci. Nurs. 32, 7–13.

Issa, R.A., Basheti, I.A., 2016. Herbal products use among chronic patients and its impact on treatments safety and efficacy: a clinical survey in the Jordanian field. Trends Med. Res. 12, 32–44.

Jonsson, A.K., Spigset, O., Tjaderborn, M., Druid, H., Hagg, S., 2009. Fatal drug poisonings in a Swedish general population. BMC Clin. Pharm. 9, 7. https://doi.org/10.1186/1472-6904-1189-1187.

Juurlink, D.N., Mamdani, M., Kopp, A., Laupacis, A., Redelmeier, D.A., 2003. Drug-drug interactions among elderly patients hospitalized for drug toxicity. JAMA 289, 1652–1658. 1610.1001/jama.1289.1613.1652.

Kanagala, V.S., Anusha, A., Rao, B.S., Challa, S.R., Nalla, K.S., Gadde, R.S., 2016. A study of medication-related problems in stroke patients: a need for pharmaceutical care. J. Res. Pharm. Pract. 5, 222–225. 210.4103/2279-4042X.185750.

Khalil, V., Li, M., Hua, Q.A., 2015. An audit of the pharmacological management of ischaemic stroke patients in a metropolitan Australian hospital. Int. J. Clin. Pharm. 37, 8–11. 10.1007/s11096-11014-10035-11096.

Kronish, I.M., Diefenbach, M.A., Edmondson, D.E., Phillips, L.A., Fei, K., Horowitz, C.R., 2013. Key barriers to medication adherence in survivors of strokes and transient ischemic attacks. J. Gen. Intern. Med. 28, 675–682. https://doi.org/10.1007/s11606-012-2308-x.

Laaksonen, R., Duggan, C., Bates, I., 2010. Performance of community pharmacists in providing clinical medication reviews. Ann. Pharmacother. 44, 1181–1190.

Lakshmi, R., James, E., Kirthivasan, R., 2013. Study on impact of clinical pharmacist's interventions in the optimal use of oral anticoagulants in stroke patients. Ind. J. Pharm. Sci. 75, 53–59. https://doi.org/10.4103/0250-4474X.113550.

Lexi-Comp, Inc., 2013. Lexi-comp's drug information handbook. 22 edition (March 2013). Hudson, Ohio: Lexi-Comp, Inc.; 2013. ISBN: 978-1591953197.

Lindblad, A.J., Howorko, J., 2008. Integration of a pharmacist into a stroke prevention clinic team. Can. J. Hosp. Pharm. 61, 431–436.

McAlister, F.A., Majumdar, S.R., Padwal, R.S., Fradette, M., Thompson, A., Buck, B., Dean, N., Bakal, J.A., Tsuyuki, R., Grover, S., Shuaib, A., 2014. Case management for blood pressure and lipid level control after minor stroke: prevention randomized controlled trial. CMAJ 186, 577–584. https://doi.org/10.1503/cmaj.140053.

McFarlane, S.I., Sica, D.A., Sowers, J.R., 2005. Stroke in patients with diabetes and hypertension. J Clin Hypertens (Greenwich) 7, 286–292.

Morisky, D.E., Green, L.W., Levine, D.M., 1986. Concurrent and predictive validity of a self-reported measure of medication adherence. Med. Care 24, 67–74.

Mozaffarian, D., Benjamin, E.J., Go, A.S., Arnett, D.K., Blaha, M.J., Cushman, M., Das, S.R., de Ferranti, S., Despres, J.P., Fullerton, H.J., Howard, V.J., Huffman, M.D., Isasi, C.R., Jimenez, M.C., Judd, S.E., Kissela, B.M., Lichtman, J.H., Lisabeth, L.D., Liu, S., Mackey, R.H., Magid, D.J., McGuire, D.K., Mohler 3rd, E.R., Moy, C.S., Muntner, P.,

Mussolino, Nasir, K., Neumar, R.W., Nichol, G., Palaniappan, L., Pandey, D.K., Reeves, M.J., Rodriguez, C.J., Rosamond, W., Sorlie, P.D., Stein, J., Towfighi, A., Turan, T.N., Virani, S.S., Woo, D., Yeh, R.W., Turner, M.B., 2006. Heart disease and stroke statistics-2016 update: a report from the american heart association. Circulation 133, e38–e360.

Pfister, B., Jonsson, J., Gustafsson, M., 2017. Drug-related problems and medication reviews among old people with dementia. BMC Pharmacol Toxicol. 18, 52. https://doi.org/10.1186/s40360-40017-40157-40362.

Qunaibi, E., Basheti, I.A., Hamadi, S.A., Bulatova, N.R., Shanah, A., Abu-Gharbieh, E., 2013. Effect of divergence in patients' socioeconomic background on their perspective of the role of the community pharmacist in Amman, Jordan. Trop. J. Pharm. Res. 12, 247–253.

Rafsten, L., Danielsson, A., Sunnerhagen, K.S., 2018. Anxiety after stroke: a systematic review and meta-analysis. J. Rehabil. Med. 5, 16501977–16502384.

Ramalho de Oliveira, D., Brummel, A.R., Miller, D.B., 2010. Medication therapy management: 10 years of experience in a large integrated health care system. J. Manag. Care Pharm. 16, 185–195. 2010(16)3: 185-195 [pii] 10.18553/jmcp.2010.16.3.185 [doi].

Roughead, E.E., Barratt, J.D., Gilbert, A.L., 2004. Medication-related problems commonly occurring in an Australian community setting. Pharmacoepidemiol Drug Saf. 13, 83–87.

Shi, Y., Yang, D., Zeng, Y., Wu, W., 2017. Risk factors for post-stroke depression: a meta-analysis. Front. Aging Neurosci. 9, 218. https://doi.org/10.3389/fnagi.2017.00218.

Silva-Smith, A., 1994. Reducing the risk of stroke in patients with chronic, nonvalvular atrial fibrillation. Nurse Pract 1994 (19), 38–39.

Sookaneknun, P., Richards, R.M., Sanguansermsri, J., Teerasut, C., 2004. Pharmacist involvement in primary care improves hypertensive patient clinical outcomes. Ann. Pharmacother. 38, 2023–2028. https://doi.org/10.1345/aph.1D605.

Sorensen, L., Stokes, J.A., Purdie, D.M., Woodward, M., Elliott, R., Roberts, M.S., 2004. Medication reviews in the community: results of a randomized, controlled effectiveness trial. Br. J. Clin. Pharmacol. 58, 648–664.

Straus, S.E., Majumdar, S.R., McAlister, F.A., 2002. New evidence for stroke prevention: scientific review. JAMA 288, 1388–1395.

Sturm, J.W., Donnan, G.A., Dewey, H.M., Macdonell, R.A., Gilligan, A.K., Srikanth, V., Thrift, A.G., 2004. Quality of life after stroke: the North East Melbourne Stroke Incidence Study (NEMESIS). Stroke 35, 2340–2345. 2310.1161/2301.STR.0000141977.0000118520.0000141973b.

Sweis, N.J., Chaloupka, F.J., 2014. The economics of tobacco use in Jordan. Nicotine Tob Res. 16, S30–S36. 10.1093/ntr/ntt1058.

Tahaineh, L.M., Wazaify, M., Albsoul-Younes, A., Khader, Y., Zaidan, M., 2009. Perceptions, experiences, and expectations of physicians in hospital settings in Jordan regarding the role of the pharmacist. Res. Social. Adm. Pharm. 5, 63–70. https://doi.org/10.1016/j.sapharm.2008.1005.1003.

The Royal Pharmaceutical society, Medicines Use Review. (Available online at: http://www.rpharms.com/health-campaigns/medicines-use-review.asp Accessed March 2018).

Tuomilehto, J., Rastenyte, D., 1999. Diabetes and glucose intolerance as risk factors for stroke. J. Cardiovasc. Risk 6, 241–249. https://doi.org/10.1177/204748739900600409.

Valderas, J.M., Starfield, B., Sibbald, B., Salisbury, C., Roland, M., 2009. Defining comorbidity: implications for understanding health and health services. Ann. Fam. Med. 7, 357–363. 310.1370/afm.1983.

Williams, L.S., Ghose, S.S., Swindle, R.W., 2004. Depression and other mental health diagnoses increase mortality risk after ischemic stroke. Am. J. Psychiatry 161, 1090–1095. 1010.1176/appi.ajp.1161.1096.1090.

Williams, L.S., Weinberger, M., Harris, L.E., Clark, D.O., Biller, J., 1999. Development of a stroke-specific quality of life scale. Stroke 30, 1362–1369.

World Health Organization 2003, Adherence to long-term therapies: evidence for action. Sabaté E, ed. Geneva : World Health Organization; 2003. (Available online at: http://www.who.int/chp/.knowledge/publications/adherence_introduction.pdf. Accessed June 2018).

World Health Organization 2018, Stroke, Cerebrovascular accident. (Available online at: http://www.emro.who.int/health-topics/stroke-cerebrovascular-accident/index.html. Accessed March 2018).

Wu, J.Y., Leung, W.Y., Chang, S., Lee, B., Zee, B., Tong, P.C., Chan, J.C., 2006. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. BMJ 333, 522. 510.1136/bmj.38905.447118.447112F.