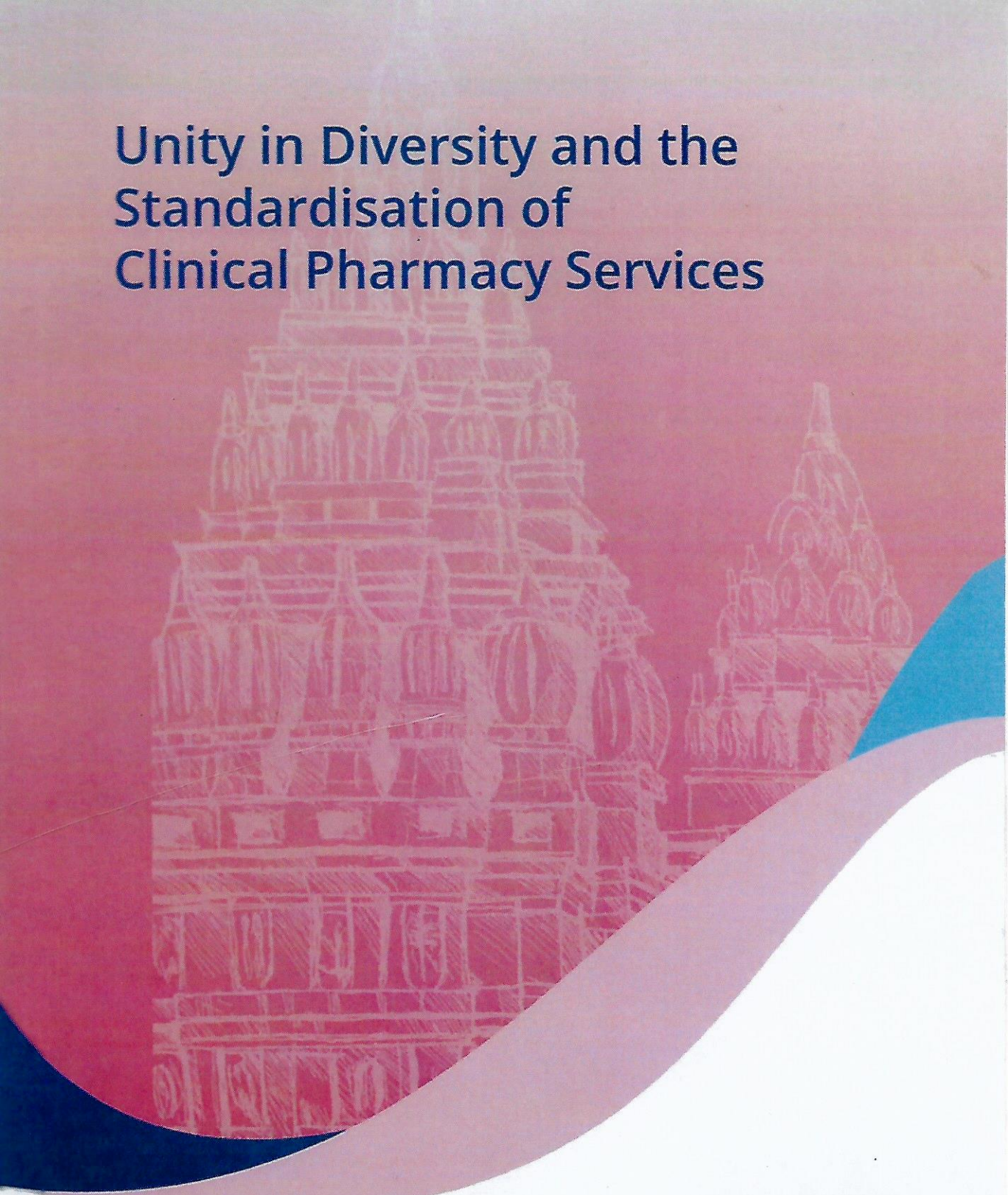
Unity in Diversity and the Standardisation of Clinical Pharmacy Services



Editors: Elida Zairina, Junaidi Khotib, Chrismawan Ardianto, Syed Azhar Syed Sulaiman, Charles D. Sands III and Timothy E. Welty

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UNITY IN DIVERSITY AND THE STANDARDISATION OF CLINICAL PHARMACY SERVICES

PROCEEDINGS OF THE 17TH ASIAN CONFERENCE ON CLINICAL PHARMACY (ACCP 2017), 28–30 JULY 2017, YOGYAKARTA, INDONESIA

Unity in Diversity and the Standardisation of Clinical Pharmacy Services

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Unity in Diversity and the Standardisation of Clinical Pharmacy Services – Zairina et al. (Eds)
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Preface

The original idea of ACCP came from Asian pharmacists who were looking for a practical conference at which they could exchange and share ideas on the concept of clinical pharmacy. In 1996, representatives from China, Korea, Japan, and USA met in Seoul, Korea to plan for the first conference. As a result, the first East Asia Conference on Developing Clinical Pharmacy Practice and Clinical Pharmacy Education (EACDCPPE) was held in America in 1997. Only 36 representatives attended and pioneers planned it as bi-annual meeting.

In 1999, the second EACDCPPE was successively held in Shanghai. This conference enabled more representatives in Asian countries to realize the differences between Asian and Western countries in the development of clinical pharmacy. When the third conference was held in Japan in 2003, the title of the conference was changed to Asian Conference on Clinical Pharmacy (ACCP). This opened the conference to more Asian countries; also the subject of clinical pharmacy was more strengthened. With a series of other Asian countries such as Philippines, Indonesia, Singapore, and so on attending ACCP, as well as with the rapid development of clinical pharmacy in Asia, every country was enthusiastic about attending and holding this conference. At the 5th conference in Malaysia in 2005, the decision was made among the representatives of the member countries to hold the conference annually instead of biannually for efficiency and convenience in regard to communicating and sharing about clinical pharmacy.

During the past 20 years, ACCP has been a major event in the clinical pharmacy scope in Asia and has been conducted in various countries especially in Asia. Clinical pharmacists have attended this prestigious meeting to share their experience in the fields of practice, research, and education on clinical pharmacy. Clinical pharmacist experts from USA, Canada, Australia, and UK have continuously come to transfer their knowledge and shared advance clinical pharmacy practice experiences. This conference supports rapid knowledge and experience transfer and enhances the emergence of clinical pharmacy practice in Asia.

Indonesia hosted the 8th ACCP in Surabaya in 2008, and again this year Indonesia has successfully hosted the 17th ACCP in Yogyakarta from 28th to 30th July 2017. This year's conference was also a celebration of 20 years of ACCP with the theme "Unity in Diversity and the Standardisation of Clinical Pharmacy Services." At ACCP 2017, there were 6 preconference workshops, poster sessions consisted of 199 posters, 21 oral presentation sessions consisted of a total of 142 oral presentations, and there were symposiums with 47 speakers, 2 plenary sessions with 4 speakers and 4 keynote speeches regarding various current issues in clinical pharmacy. About 1,133 participants attended the conference from 16 different countries.

This ACCP 2017 proceeding provides an opportunity for readers to engage with selected papers presented at the 17th ACCP 2017. This book is also a valuable contribution to gaining a better understanding about the development of clinical pharmacy particularly in Asian countries and the future global challenges. Readers will find a broad range of research reports on topics of clinical pharmacy, social and administrative pharmacy, pharmacy education, pharmacoeconomics, pharmacoepidemiology and other topics in pharmacy. The readers will also discover both common challenges and creative solutions emerging from diverse settings in developing clinical pharmacy services.

The editors would like to thank all those who have contributed to submit full papers for this 17th ACCP conference. We received 119 papers from the conference and after a rigorous peer-review, 68 papers were accepted for publication in this proceeding of which 56 are from Indonesia and 12 from Australia, Malaysia, the Philippines, and Thailand. We would like to express our special appreciation and sincere thanks to the scientific committee and the reviewers who have selected and reviewed the papers, and also the technical editor's team (Ms Arie Sulistyarini and Ms Muffarihah) who helped carry out the page layout and check the consistency of the papers with the publisher's template. It is a great honour to publish selected papers in this proceeding by CRC Press/Balkema (Taylor & Francis Group). Our special gratitude goes to the steering committee, the chairman of the conference and the members of the organizing committee involved in preparing and organizing the conference. Finally, we would like to thank Universitas

Airlangga, Indonesian Pharmacist Association, Universitas Gadjah Mada, Universitas Ahmad Dahlan, Universitas Islam Indonesia, Universitas Muhammadiyah Yogyakarta and Universitas Sanata Dharma for their endless support during the conference. Last, but not least, we also place on record our sense of gratitude to one and all who, directly or indirectly, have lent a helping hand to this conference.

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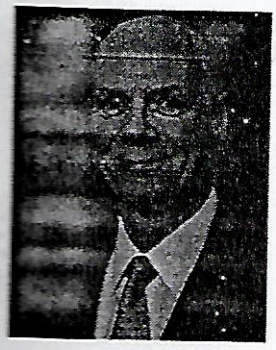
Keynote speakers

Prof. Nila Djuwita F. Moeloek—*Minister of Health, Republic of Indonesia*

Prof. Nila Djuwita F. Moeloek is a professor at the Faculty of Medicine, Universitas Indonesia (FMUI) since 1980. She graduated as Medical Doctor from FMUI in 1968. She then started her specialty in the field of ophthalmology in Rumah Sakit Cipto Mangunkusumo (RSCM) in 1979–1988. At the same time, she also became the Coordinator of Research in Department of Opthamology, FMUI—RSCM. In 2008–2009, she was chosen as the head of Medical Research Unit FMUI—RSCM. She is also well-known in the international world, as a member as well as an editor of Orbita International Magazine since 1985 to present. Currently she is the Minister of Health of Indonesia in President Joko Widodo's Cabinet.

Prof. Lilian M. Azzopardi—*Head, Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Malta*

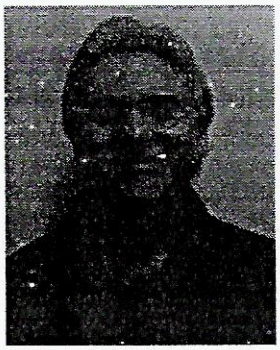
Prof. Lilian M. Azzopardi studied pharmacy at the University of Malta, Faculty of Medicine and Surgery and in 1994 she took up a position at the Department of Pharmacy, University of Malta. Prof. Azzopardi is the Head of School of Pharmacy at the University of Malta and co-ordinates the teaching of pharmacy practice. She has spearheaded major developments in pharmacy education within the University of Malta including the development of a post-graduate doctorate in pharmacy offered by the University of Malta in collaboration with the University of Illinois at Chicago. She has been invited as an external examiner for postgraduate degrees in different schools of pharmacy internationally. Her research portfolio is in the area of pharmacy quality systems and pharmacist interventions in clinical settings. She has published several papers and has been invited to give lecturers and short courses in several universities. She has received awards by the International Pharmaceutical Federation (FIP) and the European Society of Clinical Pharmacy. In 2014 she was elected as President of the European Association of Faculties of Pharmacy. She was co-chair of the working group of the FIP Nanjing Statements on Pharmacy and Pharmaceutical Sciences Education launched in 2016.



Prof. Joseph T. DiPiro—*Dean, Professor and Archie O. McCalley Chair at the Virginia Commonwealth University School of Pharmacy, Richmond, Virginia, USA*

Prof. Joseph T. DiPiro is Dean, Professor and Archie O. McCalley Chair at the Virginia Commonwealth University School of Pharmacy, Richmond, Virginia, USA. He received his BS in pharmacy (Honors College) from the University of Connecticut and Doctor of Pharmacy from the University of Kentucky. He served a residency at the University of Kentucky Medical Center and a fellowship in Clinical Immunology at Johns Hopkins University. He is President of the American Association of Colleges of Pharmacy and Past Chair of the Council of Deans. He has also served as President of the American College of Clinical Pharmacy. In 2002, he received the AACP

Robert K. Chalmers Distinguished Educator Award. He has also received the Russell R. Miller Literature Award and the Education Award from ACCP. In 2013 he was the national Rho Chi Distinguished Lecturer. Dr. DiPiro was elected a Fellow in the American Association for the Advancement of Science. Dr. DiPiro Is a past Editor of The American Journal of Pharmaceutical Education. He is an editor for Pharmacotherapy: A Pathophysiologic Approach, now in its 10th edition. He is also the author of Concepts in Clinical Pharmacokinetics and Editor of the Encyclopedia of Clinical Pharmacy. He has published over 200 journal papers, books, book chapters, and editorials in academic and professional journals.



Prof. Charles F. Lacy—*Professor of Pharmacy Practice and Vice President of Roseman University of Health Sciences, Henderson, Nevada, USA*

Prof. Charles F. Lacy, Pharm.D., MS., FASHP, FCSHP, BCPP, CAATS is Professor of Pharmacy Practice and Vice-President of Roseman University of Health Sciences. He co-founded the university with his co-founders, Dr. Renee Coffman (President) and Dr. Harry Rosenberg (President emeritus). He has practiced clinical pharmacy and taught at numerous universities over the past 35 years. He was the Clinical Coordinator of Pharmacy Services at Cedars-Sinai for 20 years. He has specialized in numerous areas over the years, including psychiatric and neurologic pharmacy, oncology and informatics. He is the lead author of the renowned "Drug Information Handbook" and lead editor of the Lexi-Comp Clinical Reference Library. Dr. Lacy is a recognized leader in Pharmacy- he has worked with numerous Pharmacy & Therapeutics (P&T) Committees at the state and national level, and has lead focus groups and task-forces in the areas of pharmacoeconomics, team building, complementary medicine, and medication therapy management throughout much of the world.

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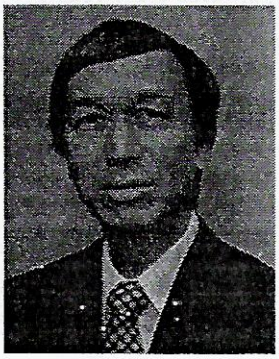
Plenary speakers

Prof. Michael D. Katz—*Professor at Department of Pharmacy Practice & Science, The University of Arizona College of Pharmacy, USA*

Prof. Michael D. Katz is Professor at the University of Arizona College of Pharmacy Department of Pharmacy Practice & Science. He practices at the University of Arizona Medical Center within the Department of Internal Medicine, His practice interests include general internal medicine, endocrinology, HIV/AIDS, infectious diseases, and evidence-based practice. Dr. Katz teaches pharmacy and medical students in both the classroom and experiential settings. He was selected in 2001 as a Dean's Teaching Scholar by the Arizona Health Sciences Center and has received numerous teaching awards. He is a Past-Chair of the American Society of Health-System Pharmacists (ASHP) Commission on Therapeutics. Dr. Katz has numerous publications and including Pharmacotherapy Principles and Practices Study Guide: A Case-Based Care Plan Approach, now in its fourth edition. Dr. Katz is the Internal Medicine PGY2 Residency Program Director and directs all residency-related activities for the College of Pharmacy. He has been involved in international education and practice for even 15 years and he serves as the College of Pharmacy's Director of International Programs. In 2010 he received the University of Arizona's prestigious Excellence in International Education Award. He has consulted and lectured extensively in Japan and many other countries regarding pharmacy education and clinical pharmacy practice and he serves as the Co-Chair of the Board of Directors of the U.S—Thai Pharmacy Consortium. Dr. Katz directs the largest program of its kind to train clinical pharmacy faculty members from Saudi Arabia.

Dr. Umi Athiyah—*A/Prof of Department of Pharmacy Practice and Dean of Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia*

Dr. Umi Athiyah is the current dean of Faculty of Pharmacy at University of Airlangga, Indonesia. Dr. Athiyah teaches various subjects including Pharmaceutical Philosophy, Community Pharmacy, Law and Ethics in Pharmacy, Management of Pharmacy Services and Logistics, Professional Communication, Pharmacoeconomics, Information Technology and Pharmaceutical Marketing. She has a research interest in Pharmacy Practice and Health Care System. She has been involved in many community based services. She has been invited as a speaker both in national and international conferences. She is one of the co-authors of a Pharmacy Management handbook.



Prof. Alan Lau—*Professor of Pharmacy Practice and Director of International Clinical Pharmacy Education at the University of Illinois at Chicago (UIC) College of Pharmacy, USA*

Prof. Alan Lau is Professor of Pharmacy Practice and Director of International Clinical Pharmacy Education at the University of Illinois at Chicago (UIC) College of Pharmacy. He obtained his Bachelor of Science in Pharmacy and Doctor of Pharmacy degrees at the State University of New York at Buffalo and then completed a clinical pharmacy residency at UIC. He pioneered the development of clinical pharmacy services for renal failure patients on dialysis. Dr. Lau had obtained many research grants for clinical and laboratory research in renal pharmacotherapeutics and clinical pharmacology, with a recent focus on mineral and bone disorder in chronic kidney disease. He has published many research papers and book chapters, including chapters in the textbooks Pharmacotherapy, Applied Therapeutics—The Clinical Use of Drugs and Basic Skills in Interpreting Laboratory Data. Dr. Lau was one of the founding members of the Nephrology Practice and Research Network of the American College of Clinical Pharmacy. In addition, he had served on the Board of Director and as Chairman of the Renal Scientific Section in the American Society for Clinical Pharmacology and Therapeutics. Dr. Lau was elected to be vice-chairman of the Nephrology/Urology Expert Committee of United States Pharmacopeia (USP) in 2007. In 2010, he was elected as a Distinguished Practitioner to the National Academies of Practice in Pharmacy. Since 2011, Dr. Lau has been working with the American College of Clinical Pharmacy on international program development and is now the International Program Director. He also has been appointed guest professor/faculty at the National Taiwan University, University of Hong Kong, University of Malta and also the Central South University in Changsha, China. Dr. Lau has been invited to give lectures on pharmacotherapy and clinical pharmacy service development in many countries, including Japan, South Korea, China, Hong Kong, Taiwan, Thailand, Vietnam, Malaysia, Singapore, Philippines, Indonesia, Saudi Arabia, Turkey and Malta.

Prof. Roger Lander—*Professor of Pharmacy Practice at Samford University, in Birmingham, Alabama, USA*

Prof. Roger Lander currently serves as Professor of Pharmacy Practice at Samford University, in Birmingham, Alabama, USA. He received his B.S.in Pharmacy and Pharm.D. from the University of Missouri-Kansas City and completed a clinical pharmacy residency program at Truman Medical Center. He then served as a faculty member at UMKC's Schools of Medicine and Pharmacy. Moving to Samford in 1986, he has developed practices in adult medicine, nutrition, ambulatory care, and pharmacokinetics. He previously served as Vice-Chair, Chair and Assistant Dean for Practice Programs. In 1994, Professor Lander helped develop a clerkship for Samford students at Guy's and St. Thomas' Hospitals in London and assisted the pharmacy there in the development of their ambulatory anticoagulation services. Professor Lander helped establish Samford's faculty/student exchange program with Meijo University in Nagoya, Japan and has traveled widely throughout Asia for information exchange and to assist colleges and hospitals in their clinical teaching and practice. He helped develop study opportunities at Samford for pharmacists from England, Japan, Korea, China, Malaysia, Indonesia, and Vietnam. Dr. Lander is one of the founders of the Asian Conference on Clinical Pharmacy. He has traveled to Indonesia at least a dozen times to assist pharmacists in their practice development.

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List of symposium speakers

SYMPOSIUM 1: DEVELOPING CLINICAL PHARMACY

Prof. Charles D. Sands—*Former Dean and Professor (retired), McWhorter School of Pharmacy, College of Health Sciences, Samford University, Birmingham, Alabama, USA*
Dr. Surakit Nathisuwan—*Associate Professor in Clinical Pharmacy in Clinical Pharmacy Division, Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand*
Ms. Nor Hasni Bt Haron—*Senior Principal Assistant Director Pharmaceutical Services Division, Ministry of Health of Malaysia*
Dr. Budi Suprapti—*A/Prof at Department of Clinical Pharmacy, Faculty of Pharmacy, Universitas Airlangga. Head of Pharmacy Department at Universitas Airlangga Teaching Hospital, Surabaya, Indonesia*
Dr. Margaret Choye—*Clinical Assistant Professor at College of Pharmacy, the University of Illinois at Chicago, USA. Clinical Pharmacist in Internal Medicine at the University of Illinois at Chicago Hospital and Health System, USA*

SYMPOSIUM 2: ADVANCED PRACTICE 1

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Medication management system in several care homes in Surabaya

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ABSTRACT: In this cross-sectional study, we aimed to observe the medication management system in several care homes in Surabaya. A total of five care homes for the elderly participated in this study. There were 196 residents and 25 caregivers who agreed to participate in this study. The abilities of the residents to read the drug label, open the strip and blister of the medicine, open a bottle of liquid medicine, and measure the liquid medicine were 53.6%, 62.2%, 70.4%, 58.7%, and 28.1%, respectively. The storage conditions met the requirement, and all medicines were disposed after their expiry dates. Of the five care homes, one was practicing improper disposal of expired medicines. These practices have severely affected the medication management system of care homes. However, there are much scope for improvement especially in caregiver skills and residents' ability to manage medication.

1 INTRODUCTION

Physiological changes experienced by the elderly make them susceptible to health problems, such as hypertension, diabetes mellitus, chronic bronchitis, decreased muscle strength, and other health disorders (Harman 1990). In 2013, results of a Health Research showed that the prevalence of diabetes in East Java is 2.5% (total sample = 1,027,763), 12.8% of whom are in the age group ≥55 years, whereas the prevalence of hypertension is 26.2%, with 75.3% in the age group of ≥55 years. This situation requires improving long-term healthcare needs that focus on improving quality of life for the elderly.

A study conducted by Hoirun Nisa (2006) in several care homes for the elderly in Jakarta found that 77.47% of respondents (total 182 respondents) had health problems, most commonly headaches (41.84%), while 57.14% of respondents had a comorbid disease, with hypertension being the most prevalently found health issue in most respondents (53.85%). Another study in Tresna Werdha Khusnul Khotimah care home in Pekanbaru found that all residents were experiencing at least one health problem, such as arthritis, gout, hypertension, hypotension, pulmonary disease, asthma, gastritis, cataracts, or dermatitis (Zulfitri 2011). As a consequence, the elderly received drug therapy.

Marek and Antle reported that the elderly have poor self-medication management, which is often associated with their poor eyesight and limited movement. A study found that 28% of the elderly did not close the pill bottles tightly so as to open them easily the next time, while 47% admitted difficulty reading the label due to poor eyesight, meaning they were not able to read the instructions in English or because the font size was too small (Marek & Antle 2008). Meanwhile, studies on three nursing homes in the Netherlands with 180 residents found that the most common causes of drug use error was the lack of supervision of nurses on drug use by the elderly, with nursing errors undermining the fact that the drugs should be taken with a glass of water. Other causes found included inappropriate time to take medication, such as 1 h early or later (Van den Bemt et al. 2009).

Care home facilities and services provided will have an impact on efforts to improve the health status of the elderly and eventually improve their quality of life. One of the main reasons that affect the quality of service is the number of caregivers provided and their level of education. The responsibilities of a caregiver are to help the elderly in performing daily activities and managing their medication. Research conducted by The Care Homes Use of Medicines (CHUMS) showed that number of staff and their skillset and training may be an important determinant of the misuse of drugs.

On the basis of the above considerations, this study aimed to identify the medication management profile of the elderly in several care homes in Surabaya, including how they obtain, use, store, and dispose the drug. We also observed the profile of caregivers as well as their involvement in managing the medication for the elderly.

2 METHODS

This was a cross-sectional and observational study with data retrieval method being a non-guided interview. This study was conducted in five care homes for the elderly in Surabaya, and the respondents were the residents and caregivers.

The variables of this study include:

1. Information related to patient demographics, namely gender, age, education level, number of health problems in the past week, and the number of drugs used in the past week;
2. Related information of caregiver demographics are gender, age, and education level;
3. How to get medication;
4. How to use the drug; in this case, the ability to use drugs, including the ability to open a bottle of medicine, open a strip and blister of the medicine, pour and measure the liquid preparation, as well as to read the drug label;
5. How to store drugs;
6. How to dispose unused medicine.

Sociodemographic data were obtained through a questionnaire that explored how the personal conditions of both the elderly and the caregiver can affect the elderly's medicine management. In addition, we also used an instrument in the form of an interview guide containing open-ended questions, which reflected on the management of daily medication by the elderly as well as caregivers. The interview results were written in a data-processing sheet to be analyzed using descriptive statistics tools such as SPSS software ver.17 and Microsoft Excel 2010.

3 RESULTS AND DISCUSSION

Data were validated with such content and by expert review. The questionnaire was then revised on the advice of these experts who were lecturers in the Faculty of Pharmacy, Universitas Airlangga. The interviewers were trained before collecting data. Questionnaires were tested on 26 respondents consisting of 6 elderly and 20 caregivers, and all questions could be easily understood by the study subjects.

As shown in Table 1, care homes were divided into three groups, namely publicly owned (care home C), privately owned for-profit organizations (care homes A and D), and privately owned non-profit organizations (care homes B and E). In publicly owned and privately owned for-profit organizations, the medication management was conducted by care home staff, whereas in privately owned non-profit organizations, the majority of medication management was conducted by the residents themselves. The ratio of residents to caregivers varied, ranging from 1 caregiver for 5 residents to 1 caregiver for 13 residents. None of the care homes trained their caregivers in managing residents' medication.

Table 1. Profile of care homes.

Care home profile		(%)
Type of care home ownership	Public	1 (20)
	Private for-profit organizations	2 (40)
	Private non-profit organizations	2 (40)
Type of care	Residential only	1 (20)
	Nursing only	0
	Mixed	4 (80)
Number of residents (person)	Care home A	71
	Care home B	29
	Care home C	50
	Care home D	39
	Care home E	20
Number of caregivers (person)	Care home A	12
	Care home B	3
	Care home C	10
	Care home D	3
	Care home E	2
Ratio of residents to caregiver (person)	Care home A	6:1
	Care home B	10:1
	Care home C	5:1
	Care home D	13:1
	Care home E	10:1
Medication management	Caregiver only	2 (40)
	Resident only	0
	Mixed	3 (60)
Training for caregivers	Available	0
	Not available	5

A total of 196 residents agreed to participate in this study. Characteristics of the residents are presented in Table 2. The majority of residents were female (76.5%), and 34.7% were aged 60–70 years. A proportion of 50% of residents had low education and 15% were illiterate. These conditions may have contributed to the number of inappropriate self-medication management practices among them.

According to Table 2, residents had experienced one to six health problems in the preceding week, and the average number of health problems found in one resident was 2. The decline in physiological function in the elderly makes them susceptible to disease and stress (Harman 1990, WHO 2016).

The increasing number of diseases has encouraged the use of drugs in the elderly. As can be seen in Table 2, it is known that 174 out of 196 residents (88.8%) have used medicine, and the average number of medicine taken by one resident was 3 in

Table 2. Characteristics of the residents.

Residents' characteristics		n (%)
Gender (n = 196)	Male	46 (23.5)
	Female	150 (76.5)
Age (years), (n = 196)	Unknown	18 (9.2)
	60–70	68 (34.7)
	71–80	48 (24.5)
	81–90	49 (25.0)
	91–100	12 (6.1)
	101–110	0 (0)
	111–120	1 (0.5)
Mean no. of health problems per resident (95% CI)		1.8(1.3–2.3)
Median no. of health problems per resident (range)		4 (1–6)
Mean no. of medicines per resident (95% CI)		3(2.5–3.5)
Median no. of medicines per resident (range)		5 (1–9)
Medication management (n = 174)*	Self	19 (10.9)
	Caregiver	155 (90.2%)
Medicine and how to obtain it (n = 670) (%)	Non-prescription	94 (14.0%)
	Prescribed	576 (86.0%)
Level of education	Illiterate	15 (7.7)
	Not graduated from elementary school	41 (20.9)
	Elementary school	36 (18.4)
	Junior high school	21 (10.7)
	Senior high school	43 (21.9)
	College	40 (20.4)
	Total	196 (100)

*A total of 22 residents did not use any medicine.

Table 3. Health problems of the elderly.

No.	Health problems	n (%)
1	Hypertension	71 (20.4)
2	Pain	68 (19.5)
3	Hyperlipidemia	23 (6.6)
4	Dry and itching skin	22 (6.3)
5	Hyperuricemia	19 (5.5)
6	Diabetes mellitus	17 (4.9)
7	Cough and cold	17 (4.9)
8	Dementia	15 (4.3)
9	Cardiovascular disease	11 (3.2)
10	Cataract	9 (2.6)
11	Diarrhea	9 (2.6)
12	Neurodisorder	8 (2.3)
13	Mobility difficulties	7 (2.0)
14	Infectious disease	7 (2.0)
15	Mental disorder	5 (1.4)
16	Other (asthma, hearing impairment, vomiting, bone fracture, gastritis, etc.)	40 (11.5)
	Total	348 (100)*

*One resident may suffer from more than one health problem.

the past week. The higher the number of medicine a person consumes, the higher will be the drug costs, risk of drug side effects, and risk of noncompliance (Indonesian Food and Drug Supervisory Agency 2008). According to Debra et al., polypharmacy is a major risk factor for the incidence of medication error. The risk is increased by 5% for each additional medicine (Debra et al. 2008).

Almost all medicines used by the elderly were prescribed by physician (86.0%). Only a small number of drugs were non-prescription medicines (see Table 2). Usually, the non-prescription medicines were obtained from visiting family or from the caregiver (dispensary at care home).

There are more than 20 health problems experienced by the elderly in care homes. Hypertension, pain, hyperlipidemia, dry and itching skin, and hyperuricemia were the five most health problems. Another health problem experienced by the elderly is pain. Information about health problems is provided in Table 3. These findings were similar to the results of the research conducted in Pune, India, reported in 2013, with respondents aged ≥60 years (Thakur et al. 2013).

There were 4.3% of residents with dementia. Specialized knowledge and skills are necessary to deal with dementia patients. Caregiver should be trained enough to provide appropriate care for residents with dementia. Another special health condition of residents that needs debriefing skills was mental disorder (1.4%). The existence of mental disorder patients at care home was quite alarming, because they required special facilities and treatment for their mental condition. Where possible, the elderly with mental disorder was proposed to be placed in a mental hospital.

Meanwhile, of the caregivers who helped the elderly manage their medication, the majority were women aged 20 30 years (68.0%) and had a college degree in health science (Table 4). Limited financial resources and the urgent need for a caregiver at care home have led to the management of care home hiring employees with inappropriate education. There were 8% of caregivers with low education level and 20% with medium education level.

The high responsibility of a caregiver should not contradict with the knowledge and skills. Limitations in caregivers in terms of education can be overcome by training them according to their job profile. On the basis of interviews with caregivers, there has never been training in medication management practice and counseling. Health

Table 4. Demographic profile of caregivers.

Category		N (%)
Gender	Male	6 (24)
	Female	19 (76)
	Total	25 (100)
Age (years)	20–30	17 (68)
	31–40	4 (16)
	41–50	3 (12)
	51–60	0 (0)
	>60	1 (4)
	Total	25 (100)
Level of education	Not graduated from elementary school	1 (4)
	Elementary school	0 (0)
	Junior high school	1 (4)
	Senior high school	5 (20)
	College in health science	17 (68)
	College in non-health science	1 (4)
	Total	25 (100)

Table 5. Medication management system profile of care homes.

Medication management system	Availability	n
Medicine procurement procedure	Available	0
	Unavailable	5
Medicine administration procedure	Available	1
	Unavailable	4
Storage of medicine procedure	Available	0
	Unavailable	5
Disposing of medicine procedure	Available	0
	Unavailable	5
Monitored dosage system	Available	3
	Unavailable	2
Patient medication record	Available	3
	Unavailable	2
Medication administration record	Available	5
	Unavailable	0
Affiliated pharmacy	Available	1
	Unavailable	4

personnel, especially pharmacists, can play a role in improving the quality of caregivers in managing medication at care homes for the elderly.

Medication management system in care homes is shown in Table 5. In general, guidelines for procurement, storage, and disposal of medicine were not provided at care homes. Only one care home provided medicine administration procedure. However, all care homes provided medication administration record.

As explained earlier, almost all drugs for the elderly were acquired by prescription (Table 2). Most of medicines were supplied by pharmacy (89.9%).

Table 6. Physical abilities of the elderly to use medicine.

	Opening packaging n (%)			Measuring liquid medication n (%)
	Blister	Strip	Bottle	
Able	138 (70.4)	122 (62.2)	115 (58.7)	55 (28.1)
Unable	58 (29.6)	74 (37.8)	81 (41.3)	141 (71.9)
Total	196 (100)	196 (100)	196 (100)	196 (100)

Furthermore, one care home cooperated with a pharmacy for its medicine supply. Prescriptions were given to the pharmacy and then the pharmacy personnel delivered the medicines to the care home. However, the standard operation procedure in medicine procurement was unavailable at all care homes (see Table 5).

The existence of a "dispensary" in institutions for the elderly should be a concern for health professionals, especially pharmacists. On the basis of the observations of researchers, drug procurement by a large numbers of caregivers is intended to be stock at care home. Procurement involves not only over-the-counter medicine but also medicine under prescription.

The physical condition of the elderly generally declines; however, patients need to do many things when using drugs, such as opening the packaging, pouring the preparations, preparation measures, and reading the drug label. Researchers asked residents to demonstrate opening different medicine packages as mentioned previously. The result was that almost half of the respondents (46.4%) were not able to read the text on the label or information on the medicine packaging. To ensure the correctness of medicine administration, reading the label or information on the packaging of medicine is important. Reading the instructions on the label prevents patients from medicine misuse and using wrong drugs, wrong dose, and wrong indications.

Table 6 presents the physical abilities of residents to read the drug label; open medicine package in the form of strips, blisters, and bottle cap of liquid medicine; and measure liquid medicine correctly. The abilities of residents to open medication blisters, strips, and liquid bottles and to measure liquid medicines accurately were 70.4%, 62.2%, 58.7%, and 28.1%, respectively (Table 6). It is evident from the table that the most difficult medicine packaging to be opened by the elderly was bottle. For solid preparations, unpacking a strip was found to be more difficult than unpacking a blister. Meanwhile, with regard to the ability to measure liquid preparations accurately, majority of residents could not accurately measure liquid medicine. Although more than 50% of the residents were able to open medicine packaging,

the inability to practice self-medication management by the elderly was quite evident. Therefore, the roles of competent caregivers are important to help the elderly use their medicine correctly.

This study found that the majority of the elderly (88.9%) did not experience difficulty in swallowing tablets with the aid of water. Only a few needed food to swallow, and a few others required crushing the tablets to swallow. With reduced saliva, the elderly may have difficulty swallowing medicines (Harman 1990).

The storage condition met the requirement criteria and all medicines were disposed after their expiration dates; however, one out of five nursing homes was practicing improper disposal of expired medicines.

There are two types of development policy regarding drug storage in care homes. Residents are allowed to store medicines in their room, and the other policy is that all medicines should be kept and managed by the caregiver. Meanwhile, for care homes that provide flexibility for the elderly to store their own medicine, drug storage containers become redundant. At one care home, almost all the medicines for the elderly were placed in a closet in a hot and stuffy room. This condition may affect drug stability, thereby reducing their effectiveness.

Furthermore, the drugs that are retained must be managed by the elderly. This can lead to new problems, namely the possibility of any indication in the elderly due to lack of knowledge about the reuse of old medicine. Drug misuse could happen because the elderly likely have memory loss and poor vision in reading information on the medicine packaging.

Care must be taken in the reuse of old drugs, because it requires considerable knowledge of medicine to guarantee the exact indication of dosage. Drugs that are damaged or expired should be destroyed before disposal. Several care homes always check the expiry dates and destroy the drugs before disposal. On the contrary, there were some care homes that do not destroy medicines before disposing them.

Caregivers in all care homes had never received training or counseling on proper disposal of medicines. This is where the role of pharmacists is important as they should be able to provide training related to the disposal of medicines so that drug managers in the Werdha can dispose drugs that are not used in the right way.

When interviewed about drug management constraints, caregivers reported the time of taking medicines as the most common problem. The low motivation of the elderly to take medicine is also a constraint that often occurs. The difficulty of delivering drugs on time is the most reported problem by caregivers (Table 7). As explained previously, the ratio of residents to caregiver varied, ranging from 1 caregiver for 5 residents to 1 caregiver for 13 residents (Table 1). The limited number of caregivers compared to the number of elderly as well as the large number of caregiver tasks in delivering care aside from managing residents' medication, as well as the poor medication management system might be the root cause of the problems. Other constraints are presented in Table 7.

Table 7. Problems in managing medication by caregivers.

Problem	Frequency n (%)
Difficult to administer medication on time	15 (31.3)
Medicine refused to be taken by the elderly	10 (20.8)
Difficult to measure drugs (e.g., splitting tablets)	9 (18.8)
Difficult to crush tablets	6 (12.5)
Forgot to give medicine	3 (6.3)
Medicine asked by the elderly without any indication	2 (4.2)
None	3 (6.3)
Total	48 (100)

Table 8. Profile of medication errors.

Type of medication error	Who committed the error	Frequency
Inappropriate indication	Resident	10
	Caregiver	33
Inappropriate dose	Resident	9
	Caregiver	12
Wrong time	Resident	2
	Caregiver	6

Further interview found medicine administration error committed by a caregiver with low education level. Previous research found that a caregiver can make mistakes such as wrong time of medicine intake (45%) and taking other residents' medicine (52%) (Szczepura et al. 2011).

Medication error profiles are presented in Table 8. Medication errors were committed by both caregivers and residents who practiced self-medication management. Low education level, lack of training, and heavy workload of caregiver have contributed to the incidence of medication error by caregiver (Barber et al. 2009, Szczepura et al. 2011). Meanwhile, the sources of medication error committed by residents were low education level, poor physical abilities such as vision impairment, mobility difficulties, and poor cognitive abilities (Marek et al. 2008).

A special case to note in the elderly is the difficulty of motivating the elderly to take medicine,

which is the second most severe problem experienced by caregivers. Overcoming this problem requires assistance of colleagues or a psychologist to find the reasons and how to motivate the elderly to take medicine.

In general, in addition to managing drugs for the elderly, caregivers are responsible for providing care for the daily activities of the elderly, such as eating, bathing, and other activities. Because of these various activities, caregivers may be less focused in recalling the time for the elderly to take their medication or they are unable to give the medication on time. This can be solved by practicing good medication management system, especially when administering regular medicines. Creating medication administration schedule includes time for medicine administration in the morning, noon, afternoon/evening or as often as needed. Other strategy is ringing a bell as a reminder for residents to take their medicine on time.

Other obstacles such as the difficulty in dividing and crushing the tablets can be overcome by providing mortar and pestle to grind the tablet as well as measuring the tablet if the desired amount is a fraction of the tablet. This reduces drug-related dose errors as well as facilitates the elderly in swallowing their tablet/capsule dosage form.

4 CONCLUSIONS

From the ability profile of the elderly, it can be concluded that the dependence of elderly people on caregivers to use drugs is relatively high. The training required for caregivers in managing medication at care homes is aimed at: (1) improving knowledge and skills in medication management for caregivers; (2) improving the quality of the medication management system in care homes; (3) using facilities to help the elderly use their medicine, especially to open medicine packaging, measure liquid medication, and provide the right medicine at the right dose for the right resident at the right time.

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Effectiveness of decision aid on knowledge, decision conflict, and outcome in diabetic patients

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ABSTRACT: The effectiveness of medication therapy can be influenced by a patient's decision in the drug use process. A lack of knowledge about medication and therapy regimen might affect the therapeutic outcome. To support patients in the drug use process, an innovation instrument, namely Patient Decision Aid (PDA), is required. In this study, we aimed to explore the effectiveness of PDA in improving medication knowledge, helping patients in decision-making about their medication, and achieving good therapeutic outcomes. The study involved pre- and post-testing, comprising 25 patients at Rumah Diabetes at University of Surabaya. The results showed that there were significant improvements in patient medication knowledge and their blood glucose levels; however, no significant difference was observed in decision conflict. The provision of PDA successfully assisted in conveying information that was not provided by other health professionals. Furthermore, pharmacists may help patients optimize their medication and continuous follow-ups to evaluate therapeutic outcomes.

1 INTRODUCTION

Diabetes mellitus is a chronic, progressive disease characterized by elevated levels of blood glucose. Diabetes of all types can lead to complications in many parts of the body and can increase the overall risk of premature death. Countries worldwide are striving to cease the rise of diabetes, reduce diabetes-related mortality, and improve access to essential diabetes medicines and basic technologies. Effective tools are available to prevent type 2 diabetes and to improve management to reduce the complications and disease progression that can result from all types of diabetes (WHO 2016).

In general, primary healthcare practitioners in low-income countries do not have access to the basic technologies needed to help patients with diabetes manage their disease properly. Only one in three low- and middle-income countries has the basic technologies for diabetes diagnosis and management available in primary healthcare facilities (WHO 2016).

Diabetes and its complications are major causes of death and has a substantial economic impact on countries and national health systems. Most countries experience a continuous increase in diabetes. International Diabetes Federation (IDF) estimated that 1 in 10 adults will have diabetes in 2040, and 1 in 2 adults with diabetes was undiagnosed. Educational programs are needed to improve the management of people with diabetes mellitus, and public health education is needed at the population level to encourage behavior change to prevent type 2 diabetes. Countries with high prevalence of diabetes need to develop and implement cost-effective programs to improve the health outcomes of people with diabetes and prevent new cases (IDF 2015).

Indonesia ranks seventh in top 10 countries in terms of number of adults with diabetes (IDF 2015). Health systems in Indonesia have started a managed care health coverage BPJS only in 2014. Many conditions need to be improved for better control of the disease, especially in chronic care disease. Most problems in Indonesia are due to reduced access to medication and increased disease complication, especially caused by diabetes, hypertension, and cancer. A strong action is needed to promote care, prevention, and cure of diabetes mellitus, which must also play a leading role in influencing policy, increasing public awareness, and encouraging improvements in health (Indonesia Ministry of Health 2015).

Many factors may affect treatment compliance, particularly commitments to taking medication in treating the disease, concerns about side effects, and medical expenses. Patients with type 2 diabetes mellitus (DM) have a wide and diverse range of issues, which can be challenging for both doctors and patients. Several factors may affect adherence to the treatment of diabetes patients, namely knowledge of the disease, perceptions of the benefits and roles of antidiabetic drugs, treatment costs, actual or potential side effects, complex dosing regimens, and patient characteristics (Tunceli et al. 2015).

The main factor affecting the success of therapy is making treatment decisions. Therefore, to achieve

success in the treatment, it is necessary for healthcare providers to provide care, in the form of counseling and information to help patients participate in healthcare decision-making and to improve their quality of life and prevent worsening conditions and complications (Mathers et al. 2012). Therefore, an instrument or media that can promote collaboration between patients and healthcare providers, called patient decision aid (PDA), is used, which can be in the form of a leaflet, brochure, interactive media, video/DVD, or audio cassette. These media are not intended to replace patient interactions with healthcare providers, but are intended to help patients in the decision-making process (Chow et al. 2009).

The use of PDA is important because the perception of each patient may be different from the intervention of healthcare providers. PDA will help patients to increase their knowledge and understanding of information, to select the type of medicine to gain better expectations and more realistic clinical outcomes. The important role of healthcare professionals is to enhance knowledge and self-management of patient for better outcomes (ADA 2016). There are many conditions that affect patients' readiness to change after receiving an information from a health practitioner. This made the decision-making difficult for patients to use the medication appropriately to control the disease (Chow et al. 2009).

In this study, patients were made familiar with the interventional use of PDA to achieve outcomes such as increased patients' understanding of their diabetes treatment and more effective decision-making about treatment and therapeutic outcomes.

2 METHODS

A pre-experimental research design "the one-group pre-test and post-test design" was used in this study (Christensen 2010). The study population included outpatients with type 2 diabetes mellitus who used oral antidiabetic (OAD) therapy, not reached the therapeutic target, and managed by Rumah Diabetes at University of Surabaya. The sample size was 25 patients, calculated using Slovin's formula. The patients were given PDA in the form of a card as a tool to assist them in making decisions of their diabetes treatment (Stacey et al. 2006; Figure 1).

The patients were given an explanation of how to use PDA. After four weeks, the differences in patient knowledge, decision-making, and blood glucose levels were measured and analyzed using the statistical paired t-test (Figure 2).

The measuring instruments used were a medication knowledge survey (Case Management Adherence Guideline 2006), the decision conflict scale (DCS) questionnaire (O'Connor 2010), and an Accu-Chek® glucometer.

In medication knowledge survey, the following questions were asked to the patients regarding their medications (Case Management Adherence Guideline 2006):

a. List and name of the medication (Can the patient read the label? Note: Incorrect pronunciation is not considered a failure on the patient's part to identify medication.
b. Why is the medication being taken? (for what disease or condition?)
c. How much medication (number of pills) are to be taken each time?
d. When is the medication to be taken? (morning, before meals, twice a day, etc.)
e. What effects should the patient be looking for? (both positive and negative)
f. Where is the medication kept? (to ascertain special storage conditions needed)
g. When is the next refill due? (and plan or methods for obtaining refills of the medication)

The score for calculating the medication knowledge survey was to use the value of the total ratio examined from each question to the total of questions on a scale of 0 to 8. There were a total of eight answers for each drug. Code 0 denotes score of the survey <50%, which was classified as low patient medication knowledge. Code 1 denotes score of the survey >50–70%, which was classified as moderate patient medication knowledge. Code 2 denotes score of the survey >70–90%, which was classified as high patient medication knowledge. Code 3 denotes score of the survey >90%, which was classified as very high patient medication knowledge. If the patient received more than one drug, the number of drugs will be multiplied by 8. Then, the result or value was divided by the value obtained by the patient. Medication knowledge level was analyzed using the Wilcoxon matched pairs test.

The decisional conflict scale measures personal perception of uncertainty in choosing options, feeling uninformed, being unclear about personal values, being unsupported in decision-making, and making effective decisions[9].

Each part of the question consists of five ranking scores: 0 = "strongly agree"; 1 = "agree"; 2 = "doubt"; 3 = "disagree"; 4 = "strongly disagree". We calculate 16 parts of each answered question and carried out the following processes: (A) summing; (B) dividing by 16; (C) multiplying by 25. The score ranged from 0 (no decision conflict) to 100 (very high conflict). It is classified into three groups: score 0–25 was classified as good decision-making, 26–50 was classified as moderate decision-making, and >50 as low decision-making.

EFEKTIVITAS PENURUNAN GULA DARAH

CARA KERJA OBAT	GOLONGAN OBAT	NAMA OBAT	PENURUNAN HBA1C
Meningkatkan jumlah insulin	Sulfonilurea	Glibenclamid Glimepirid Gliclazid Glipizid Glikuidon	1-2%
	Glinid	Repaglinid Nateglinid	1-2%
Meningkatkan jumlah insulin & menghambat pelepasan glukagon (cadangan gula)	DPP 4 - inhibitor	Vildagliptin Sitagliptin Linagliptin Saxagliptin	0,5-0,8%
	Incretin Mimetics	Liraglutid	0,5-1%
Menekan produksi glukosa hati & menambah sensitifitas terhadap insulin	Biguanid	Metformin	1-2%
Menghambat penyerapan gula setelah makan	Penghambat glukosidase alfa	Acarbose	0,5-0,8%
Mengubah cara kerja insulin	Tiazolidindion	Pioglitazon	0,5-1,4%
Merangsang produksi glukosa hati, stimulasi pemanfaatan glukosa	Insulin	Insulin	1,5-2,5%

ATURAN PEMAKAIAN OBAT

GOLONGAN OBAT	NAMA OBAT	ATURAN PEMAKAIAN	KETERANGAN
Sulfonilurea	Glimepirid Glipizid	1x sehari 1x sehari	Diminum sesaat sebelum atau pada waktu makan yang pertama (jangan digunakan bila tidak makan)
	Glibenclamid	1-2x sehari	
	Gliclazid	2x sehari	
	Glikuidon	2-3x sehari	
Glinid	Repaglinid Nateglinid	3x sehari 3x sehari	Diminum sesaat sebelum atau pada waktu makan yang pertama (jangan digunakan bila tidak makan)
DPP 4 - inhibitor	Vildagliptin	1-2x sehari	Diminum sebelum, pada waktu atau sesudah makan (jangan digunakan bila tidak makan)
	Sitagliptin Linagliptin Saxagliptin	1x sehari 1x sehari 1x sehari	
Biguanid	Metformin	1-3x sehari	Diminum pada waktu atau sesudah makan (jangan digunakan bila tidak makan)
Penghambat Glukosidase alfa	Acarbose	1-3x sehari	Diminum pada suapan pertama makan
Tiazolidindion	Pioglitazon	1x sehari	Diminum sesudah makan
Incretin Mimetics	Liraglutid	Sesuai rekomendasi Dokter	Disuntikkan di bawah kulit
Insulin	Insulin	Sesuai rekomendasi Dokter	Disuntikkan di bawah kulit

PEMERIKSAAN GULA DARAH MANDIRI

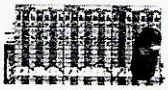
OBAT ANTIDIABETES ORAL (TABLET)

	Senin Pagi	Selasa	Rabu	Kamis Siang	Jumat	Sabtu	Minggu Malam
Sebelum makan	✔			✔			✔
2 jam Sesudah Makan	✔			✔			✔

INSULIN (INJEKSI)

	Senin Pagi	Selasa	Rabu	Kamis Siang	Jumat	Sabtu	Minggu Malam
Sebelum makan	✔	✔	✔	✔	✔	✔	✔
2 jam Sesudah Makan	✔	✔	✔	✔	✔	✔	✔

Pemeriksaan bisa lebih jarang bila gula darah sudah stabil
(Metode SMBG low intensity/mod based IDF 2009)



EFEK HIPOGLIKEMI & PERUBAHAN

GOLONGAN OBAT	NAMA OBAT	EFEK HIPOGLIKEMI	PERUBAHAN BERAT BADAN
Sulfonilurea	Glibenclamid Glimepirid Gliclazid Glipizid Glikuidon	Glibenclamid dan Glimepirid lebih sering menyebabkan hipoglikemi	Sulfonilurea rata-rata meningkatkan berat badan
Glinid	Repaglinid Nateglinid	Dapat menyebabkan Hipoglikemi	Dapat meningkatkan berat badan
DPP 4 - inhibitor	Vildagliptin Sitagliptin Linagliptin Saxagliptin	-	Tidak berkaitan dengan peningkatan berat badan
Biguanid	Metformin	-	Tidak berkaitan dengan peningkatan berat badan
Penghambat glukosidase alfa	Acarbose	-	Tidak berkaitan dengan peningkatan berat badan
Tiazolidindion	Pioglitazon	-	Tidak berkaitan dengan peningkatan berat badan
Incretin Mimetics	Liraglutid	-	Menurunkan berat badan
Insulin	Insulin	Sering menyebabkan Hipoglikemi, terutama insulin kerja pendek dan cepat	Meningkatkan berat badan

EFEK SAMPING

GOLONGAN OBAT	NAMA OBAT	EFEK SAMPING	KETERANGAN LAIN
Sulfonilurea	Glimepirid Glipizid Glibenclamid Gliclazid Glikuidon	Pada awal penggunaan dapat menimbulkan mual, gatal, diare	Pada pasien dengan gangguan fungsi hati dan ginjal, Glipizid tidak direkomendasikan
Glinid	Repaglinid Nateglinid	Mual, diare	
DPP 4 - inhibitor	Vildagliptin Sitagliptin Linagliptin Saxagliptin	Sebah, Muntah, Sakit Kepala, hidung tersumbat	Linagliptin dapat diberikan pada gangguan fungsi hati dan ginjal (tanpa penyesuaian dosis)
Biguanid	Metformin	Pada beberapa minggu pertama dapat menimbulkan gangguan pencernaan (mual, diare, kembung)	Pada pasien diabetes dengan gangguan fungsi ginjal berat tidak direkomendasikan
Penghambat Glukosidase alfa	Acarbose	Menimbulkan gangguan pencernaan (flatang angin), tinja lembek	
Tiazolidindion	Pioglitazon	Bengkak pada jari tangan, rangkai kasi karena retensi cairan	Tidak disarankan pada pasien gagal jantung dan riwayat fraktur
Incretin Mimetics	Liraglutid	Sebah, muntah, diare	
Insulin	Insulin		Perlu pemantauan gula darah ketat

PERTIMBANGAN HARGA

GOLONGAN OBAT	NAMA OBAT	HARGA	KETERANGAN
Sulfonilurea	Glibenclamid Glimepirid Glipizid Glibenclamid Gliclazid Glikuidon	Ekonomis	Sangat Efektif
Glinid	Repaglinid Nateglinid	Mahal	Sangat Efektif
DPP 4 - inhibitor	Vildagliptin Sitagliptin Linagliptin Saxagliptin	Mahal	Tidak ada kaitan dengan berat badan
Biguanid	Metformin	Ekonomis	Tidak ada kaitan dengan berat badan
Penghambat Glukosidase alfa	Acarbose	Mahal	Tidak ada kaitan dengan berat badan
Tiazolidindion	Pioglitazon	Mahal	Memperbaiki profil lipid/kolesterol
Incretin Mimetics	Liraglutid	Mahal	Dapat menurunkan berat badan
Insulin	Insulin	Mahal	Memperbaiki profil lipid/kolesterol dan sangat efektif

Figure 1. PDA cards.

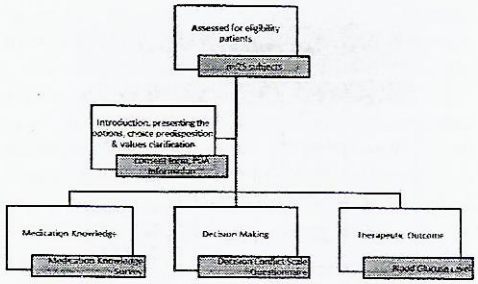


Figure 2. Flow diagram of participants.

3 RESULTS AND DISCUSSION

Interviews were conducted for 4 weeks on each patient from March to June 2016. The variables studied include independent variable such as PDA as a tool for medication aid, and dependent variables, such as patient medication knowledge, blood glucose levels, and treatment decisions using the DCS questionnaire. Patient baseline characteristics are described in Table 1.

3.1 *Medication knowledge survey after PDA administration*

Medication knowledge includes the knowledge of the name, composition, purpose, and amount of medicine at each use; the positive effects and negative effects; drug storage, and the date of next purchase of drug. PDA administration will help patients to manage their medication regimen for the beneficial outcomes. In this study, the average knowledge of the study population was good. Results of a medication knowledge survey conducted over 4 weeks after providing PDA show that all respondents had a high knowledge of the antidiabetic drugs used.

As the above results show a p value (asymptotic significance, two-tailed) of 0.003, which is less than the critical limit of the study (0.05), it can be concluded that there is a significant difference in drug knowledge between the pre- and post-PDA administration.

3.2 *Blood glucose levels after PDA administration*

In major clinical trials, the use of self-monitoring blood glucose (SMBG) for glycemic control is useful as a multifactorial intervention. In this intervention with PDA, we show that SMBG can be an effective therapy component. SMBG allows patients to evaluate their individual response to therapy and assess whether the target glycemic control is achieved or not. SMBG results can be useful in preventing hypoglycemia and

Table 1. Baseline characteristics of the patients.

Characteristics		n = 25	%
Gender	Male	19	76
	Female	6	24
Age (years)	>18–25	1	4
	26–35	1	4
	36–45	4	16
	46–55	8	32
	56–65	11	44
Duration of diabetes (years)	1–5	12	48
	6–10	8	32
	11–15	5	20

Table 2. Patients' medication knowledge after PDA administration.

Medication knowledge category	Before		After	
	Frequency	%	Frequency	%
Code 0 Low medication knowledge	0	0	0	0
Code 1 Moderate medication knowledge	3	12	0	0
Code 2 High medication knowledge	22	88	19	76
Code 3 Very high medication knowledge	0	0	6	24
Total	25	100	25	100

Table 3. Statistical analysis of patients' medication knowledge after PDA administration.

Test Statistics[b,c]			Sesudah sebelum
Z			−3.000[a]
Asymp. Sig. (2-tailed)			0.003
Monte Carlo Sig. (2-tailed)	Sig.		0.004
	95% Confidence Interval	Lower Bound	0.002
		Upper Bound	0.005
Monte Carlo Sig. (1-tailed)	95% Confidence Interval	Lower Bound	0.001
		Upper Bound	0.002
	Sig.		0.001

Table 4. Monitoring of blood glucose levels after PDA administration.

Subject no.	Week 1 (mg/dL)	Week 2 (mg/dL)	Week 3 (mg/dL)	Week 4 (mg/dL)
1	276.0	449.0	291.0	271.0
2	222.0	336.0	146.0	101.0
3	207.0	140.0	243.0	176.0
4	216.0	201.0	170.0	155.0
5	222.0	179.0	181.0	158.0
6	339.0	305.0	324.0	292.0
7	254.0	186.0	131.0	126.0
8	278.0	143.0	144.0	304.0
9	214.0	85.0	122.0	108.0
10	187.0	135.0	170.0	72.0
11	281.0	380.0	204.0	79.0
12	266.0	188.0	167.0	276.0
13	214.0	170.0	186.0	125.0
14	230.0	184.0	105.0	163.0
15	330.0	480.0	381.0	288.0
16	136.0	110.0	109.0	128.0
17	340.0	397.0	302.0	260.0
18	199.0	155.0	167.0	154.0
19	198.0	103.0	88.0	109.0
20	216.0	108.0	176.0	116.0
21	186.0	130.0	142.0	191.0
22	360.0	321.0	292.0	341.0
23	185.0	130.0	107.0	120.0
24	272.0	262.0	214.0	186.0
25	368.0	226.0	121.0	270.0

Note: Blood glucose levels were measured as random blood glucose (about 3 h after the first meal) from the capillary blood vessels using an Accu-Chek® glucometer.

Table 5. Statistical analysis of blood glucose levels after PDA administration (ANOVA).

	Sum of squares	df	Mean square	F	Sig.
Between Groups	69742.990	3	23247.663	3.176	0.028
Within Groups	702694.000	96	7319.729		
Total	772436.990	99			

in drug adjustment (especially prandial insulin dose), nutritional therapy, and physical activity. In a recent meta-analysis, it has been shown that SMBG patients with type 2 DM of OAD therapy could decrease HbA1c values by 0.25% in the first 6 months, whereas results from Cochrane review concluded that the overall SMBG effect in patients with type 2 DM was relatively down at 6 months after initiation and decreased after 12 months (Diabetes Care 2013).

Table 6. Decision conflict scale after PDA administration.

Domain	Test	Sig. value	Conclusion
Informed subscale (feeling uninformed)	*Wilcoxon matched pairs test*	0.480	No significant difference
Value clarity subscale (unclear about personal values)	*Wilcoxon matched pairs test*	0.257	No significant difference
Support subscale (unsupported in decision-making)	*Wilcoxon matched pairs test*	0.655	No significant difference
Uncertainty (personal perception of uncertainty in choosing options)	*Wilcoxon matched pairs test*	0.527	No significant difference
Effective decision subscale (effective decision-making)	*Wilcoxon matched pairs test*	0.157	No significant difference

On the basis of the above results, we show a significance of 0.028, which is less than the critical limit of the study (0.05). This means that there are significant differences between the study patients, especially in blood glucose levels before and after PDA administration.

3.3 *Decision conflict scale after PDA administration*

From the results of the research indicating that there is no significant difference between pre- and post-PDA administration, it can be concluded that decision-making may be influenced by many factors such as the delivery of PDA information to the patient and patient's condition, including emotional level and stress level with their disease condition (Branda et al. 2013). The degree of uncertainty in making decisions involving the benefits and risks of OAD also affects the decision-making of patients (Elwyn et al. 2011). On the contrary, the provision of PDA successfully assists in exploring factors that have not been investigated by doctors or other health care providers before (Chow et al. 2009), (Murray et al. 2007). For example, regarding weight change, when patients and physicians discuss weight changes in a treatment, it generally refers to the context of glycemic control rather than as a potential side effect of the drug. However, PDA also received rave reviews from research

patients as many of them had never received an explanation of OAD before.

4 CONCLUSIONS

Through PDA administration, several changes were observed in the present study patients, including increased medication knowledge and better therapeutic outcomes as observed by monitoring their random blood glucose levels. PDA will become one of the successful tools that will engage or involve patients in clarifying values and expectations that are more realistic in their medication knowledge. However, it contributes less to decision-making because the concept of PDA is still new to these study subjects.

Furthermore, to help patients participate successfully in decision-making about their treatment, the role of pharmacists is required in improving their medication knowledge and blood glucose monitoring, as well as in achieving continuous follow-ups to evaluate the treatment of type 2 diabetes mellitus.

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Self-esteem scale: Translation and validation in Malaysian adults living with asthma

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ABSTRACT: This study was undertaken to translate and validate the Rosenberg Self-Esteem Scale (RSES) for use among Malaysian adult asthma patients. A total of 152 adult asthma patients were enrolled from four respiratory clinics. The 10-item RSES was translated into Malaysian language by step-wise iterative translation procedure. After establishing the content and face validation of Malay version of RSES (RSES-M), internal consistency and test-retest reliability were assessed. The Cronbach's α and Interclass Correlation Coefficient (ICC) values were 0.781 and 0.884. Kaiser-Mayer-Olkin (KMO) value (0.681) proved the sample adequacy and Barlett's test of sphericity x2 (45) = 419.37, $p < 0.001$ indicated that correlations between items were sufficiently large for factor analysis. Moreo-ver, all values of output tables for items' construct were within the specified ranges of the Rasch model. RSES-M is a reliable and valid scale that is conceptually and psychometrically equivalent to English version.

1 INTRODUCTION

Self-esteem (SE) is often defined as personal and global feelings of self-worth, self-regard and self-acceptance (Rosenberg 1979). It is an important component of psychological health that may affect the health behaviour and disease management of the patients living with chronic illnesses (Gallant 2003). The low SE of the patients has been linked with more chances of medication non-compliance (Watson et al. 2007, Fung et al. 2008), frequent relapses of symptoms and delayed disease recoveries (Rodrigues et al. 2013). On the contrary, improvement in SE resulted in better self-management of the chronic diseases including asthma (Ahmad et al. 2014).

Previously, various researches focused on the impact of asthma on the patients' psychosocial well-being (Ritz et al. 2013). The level of SE of asthma patients may impact the control and self-management of asthma (Ahmad et al. 2014). Asthma patients may experience negative psychosocial consequences like low SE because of frequent work leaves, hospitalizations, and emergency room visits (Ahmad & Ismail 2015a), (Ahmad & Ismail, 2015b). Therefore, the suffering from asthma does not only mean deterioration of pulmonary functioning but the deterioration of social and psychological functioning also.

The SE of the patients has been assessed by using various self-administered questionnaires: mainly Rosenberg Self-Esteem Scale (RSES) (Rosenberg, 1965), Texas Social Behaviour Inventory (TSBI) (Helmreich & Stapp 1974), and Self-Esteem Inventories (SEI) (Coopersmith 1981). Among these questionnaires, the 10-item RSES has been frequently used to assess the SE of patients living with chronic illnesses (Symister & Friend 2003). In Malaysia, there is no validated tool in Malay language to assess SE of the patients. This study aimed to translate and validate the RSES-M in adult asthma patients. For this purpose, the RSES was translated in accordance to international translation standards and validated by both classical test theory (factor analysis) and modern response theory (item measures (Fit statistics) by Rasch analysis). After validation, the SE of the enrolled asthma patients was assessed from the completed RSES-M.

2 METHODS

2.1 *Ethics*

The study protocol was approved by the research management institute (Postgraduate Academic and

Ethics Committee (600-FF-(PT-9/19)) and Ministry of Health (Medical Research and Ethics Committee (MREC) (NMRR-14-557-20184)), Malaysia.

2.2 *Participants and study settings*

This cross-sectional study was conducted in four academic respiratory specialist clinics in Selangor, Malaysia. Post signed consent, 152 asthma patients (aged > 18 years old; nil cognitive disability; not diagnosed with other respiratory diseases) were recruited using purposive sampling method. Data were collected for the period of nine months: from 1st April 2014 to 30th December 2014.

All data collection processes were performed by the principle investigator. The data analyses were carried out by the Statistical Package for Social Science (SPSS®) version 21 for descriptive analysis, internal consistency, test-retest reliability and factor analysis (principle component analysis), whereas the Bond and Fox software® was used for generation of item measures for Fits statistics.

2.3 *Original instrument (Rosenburg Self-Esteem Scale)*

The permission to use and translate 10-item RSES for Malaysian population was obtained from the corresponding author (Rosenberg 1965). The enrolled asthma patients' responses were recorded on a 4-point Likert scale where response to the statement varied from strongly agree (score = 4) to strongly disagree (score = 1). Five items in the scale were reverse coded (item number: 2, 5, 6, 8, 9), for these items scoring was reversed from strongly agree (score = 1) to strongly disagree (score = 4). Higher score reflected the greater SE. Total score of 75% or above (score ≥ 30 / 40) reflected high SE, 50%–74% (score = 20–29 / 40) represented moderate and 49% or below (score < 20 / 40) reflected low SE.

2.4 *Instrument translation methodology*

A forward-backward-forward translation technique was used to translate the 10-item RSES scale. The translation process was taken by experts at the Academy of Language Studies and Respiratory Unit, Faculty of Medicine, Universiti Teknologi MARA (UiTM), Malaysia. The original English version of RSES was translated to Malay language by two independent local professional bilingual experts; one of them had linguistic background and other had clinical background. The both translated versions were reviewed by the local project manager of translation committee and agreed on a single reconciled version (reconciliation). The review of these intermediary versions was conducted by respiratory physicians.

The translated Malay version of the RSES was translated back into English to ensure the conceptual, structural and operational equivalence between these two versions. The reverse translation was done by two independent bilingual translators who were totally blind to the original version.

After harmonising the both translated versions, pre-test cognitive debriefing of the instrument was done to actively test the feasibility, interpretation, understanding, and cultural relevance among eight adult asthma patients. The enrolled patients were asked to restate the questions in their own words to catch the nuances and subtleties of responses and to discover errors and difficulties in the translated instruments. Lastly, the difficulties or confusions that were discovered during the interview stage were addressed and the translations were revised accordingly.

2.5 *Qualitative validation of RSES-M*

In content validation, dimensions, sub-dimensions and arrangement of the items to address the proper understanding of the questions to the patients were ensured. Content validation contributes to early stages of instrument development that involved identification of conceptual framework, adopting that framework to the area of interest by utilising the expertise of professionals from that field (Turner et al. 2007). In present study, the content validation was done by a senior panel comprising of three practicing respiratory physicians, two senior pharmacists and one expert in questionnaire validation.

Face validation was necessary to ensure that the statements convey the same meanings to the patients as the investigator intended. Therefore, RSES-M was administered in ten asthma patients to judge the understanding of the patients about the translated statements in the questionnaire.

3 RESULTS AND DISCUSSION

Table 1 illustrates the socio-demographic characteristics and level of SE of the enrolled asthma patients. In this study the mean age of the asthma patients was 52.03 (±15.11) years old and the number of years since diagnosed as asthmatic was 21 (±15.66) years. Majority of the patients were females (n = 107; 70.4%) and Malay (n = 81; 53.3%). The overall mean score for SE was 29.31 (±3.29) suggesting that the enrolled asthma patients had moderate level of SE.

3.1 *Reliability of RSES-M*

The RSES-M showed good internal consistency and test-retest reliability. The Cronbach's alpha

Table 1. Socio-demographic data and SE of enrolled adult asthma patients (n = 152).

Sr. #	Items	Category	Mean ± SD	n (%)
1	Gender	Male		45 (29.6)
		Female		107 (70.4)
2	Age (years)		52.03 ± 15.11	
3	Ethnicity	Malay		81 (53.3)
		Chinese		30 (19.7)
		Indian		41 (27.0)
		Others		0 (0)
4	Income per household/ month (RM)	<1000		51 (33.6)
		1000–2000		59 (38.8)
		2001–3000		23 (15.1)
		>3000		19 (12.5)
5	Number of years since diagnosed as asthmatic		21 ± 15.66	
		<5 years		27 (17.7)
		5–10 years		31 (20.4)
		>10 years		94 (61.8)
6	Self-esteem		29.31 ± 3.29	
		High		45 (29.6)
		Moderate		96 (63.1)
		Low		11 (7.2)

Table 2. Reliability analysis of RSES-M (n = 152).

Sr. #	Scale mean if item deleted	Scale variance if item deleted	Corrected item-total correlation	Cronbach's alpha if item deleted
S01	26.97	15.51	0.314	0.776
S02	27.48	14.36	0.491	0.754
S03	26.98	15.74	0.386	0.768
S04	26.95	15.41	0.432	0.763
S05	27.58	15.67	0.303	0.777
S06	27.28	12.55	0.714	0.719
S07	26.95	15.41	0.432	0.763
S08	27.28	12.55	0.714	0.719
S09	27.44	14.10	0.383	0.774
S10	27.07	15.42	0.315	0.776

value was 0.781, which surpassed the 0.70 criterion for good reliability index. The performance of each item for reliability of the whole scale is shown in Table 2.

For one month test-retest reliability, 34 asthma patients (more than one fifth of total sample) completed RSES-M two times with one month apart. The instrument appeared to have excellent test-retest reliability by Interclass Correlation Coefficient (ICC) values of 0.884. These values suggested that the instrument retained its good test-retest reliability values. These results demonstrated that the RSES-M was a reliable and stable instrument to assess the self-esteem in the enrolled asthma patients.

3.2 *Construct validation of RSES-M*

Factor analysis was conducted to group the items of RSES-M sharing same dimensions. The value of KMO test was 0.681 suggesting sample size sufficiency, while Barlett's test of sphericity x2 (45) = 419.37, $p < 0.001$ indicated that correlations between items were sufficiently large for factor analysis (Comrey & Lee 2013). The analysis of scree plot supported to retain two factors. These two factors were categorised as positive SE items and negative SE items on the basis of nature of the questions in each cluster as shown in Table 3.

Furthermore, Fits statistics for Rasch analysis was applied by using Bond and Fox software® and item measures were analysed for infit/outfit MNSQ (0.6–1.4), infit/outfit ZSTD (±2), and PTMEA Corr. (0.3–0.7) (Bond and Fox, 2013). Figure 1 illustrates the item-person map based on person ability and item difficulty.

None of the item of RSES-M violated the Rasch specification and all values were within stipulated radius of the model as reported in the Table 4.

The prime purpose of this study was to translate and document the reliability and validity of RSES-M in the sample of adult asthma patients. RSES (English) was successfully culturally adapted for Malaysian asthmatic patients. This study proved RSES-M as reliable and valid scale that is

Table 3. Summary of factor analysis results for SE items.

	1	2
Sr. #	Negative self-esteem	Positive self-esteem
S01		0.625
S02	0.729	
S03		0.735
S04		0.417
S05	0.402	
S06	0.803	
S07		0.882
S08	0.895	
S09	0.678	
S10		0.301
Eigenvalue	2.948	1.886
% age of variance explained	27.996	20.334
Cronbach's Alpha	0.771	0.647

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

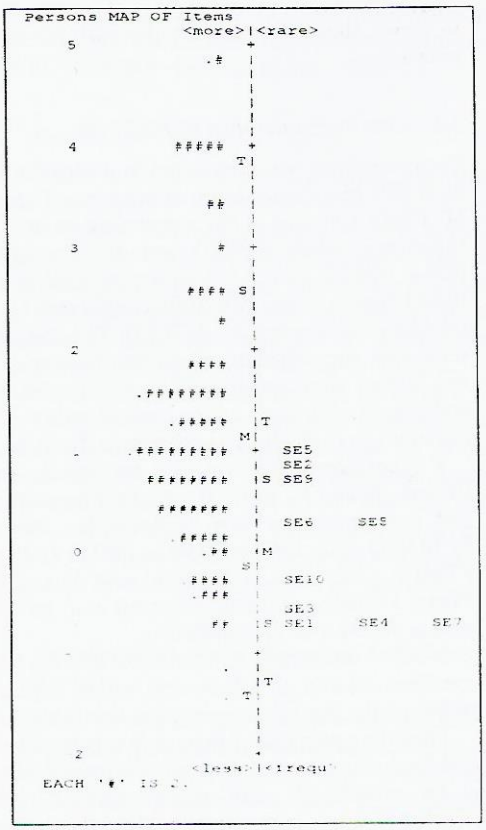

Figure 1. Item-person map based on person ability and item difficulty (n = 152).

Table 4. Rasch analysis for SE items from real study (n = 152).

Item	INFIT MNSQ	INFIT ZSTD	OUTFIT MNSQ	OUTFIT ZSTD	PTMEA
S01	1.26	1.90	1.17	1.18	0.47
S02	0.83	−1.54	1.00	0.02	0.56
S03	0.76	−2.03	0.73	−2.09	0.52
S04	0.79	−1.69	0.74	−2.02	0.57
S05	0.93	−0.63	1.04	0.41	0.42
S06	0.89	−0.90	0.83	−1.37	0.76
S07	0.79	−1.69	0.74	−2.02	0.57
S08	0.89	−0.90	0.83	−1.37	0.76
S09	1.47	1.62	1.47	2.17	0.57
S10	1.26	1.88	1.18	1.34	0.48

conceptually and psychometrically equivalent to original version (RSES), and acceptable to Malaysian asthma patients.

The RSES-M showed good internal consistency as overall scale (Cronbach's alpha = 0.781). These values indicated that the instrument was internally consistent and at least 78% of the variance in the observed scores could be attributed to variation in SE of asthma rather than measurement error. The relia-bility analysis revealed that similar to English version (RSES), the Malay version (RSES-M) also proved to be a highly reliable instrument. Previously, the internal consistency of RSES items was assessed in 53 nations simultaneously and the resultant Cronbach's α coefficient values varied from 0.61 to 0.90 (Schmitt and Allik, 2005). In Malaysia, the reported Cronbach's α value was 0.74 that was almost similar (0.781) to this present study.

One month test-retest analysis was done to test the stability and reliability of an instrument over time. The study instrument of present study was prime candidate for test-retest reliability analysis because of little chances of sudden changes in SE of asthma. The time period of one month was selected based on scheduled appointment visit to the respiratory clinics and to dampen down the chances of skewing the results. Previously, the test-retest reliability analysis was performed by King and co-workers (King et al., 2007). The finding for test-retest reliability of their study was consistent to present study. The test-retest values of both original RSES (English version) and adopted version RSES-M (Malay version) were 0.701 and 0.851 respectively, suggesting that both versions retain the stable reliability values.

The findings of factor analysis for RSES-M revealed two dimensions of the scale, one for positive worded items and another for negative worded items, implying that some individuals scored high in one dimension and low in the other. The factor structure of RSES-M (adopted version) was in accordance to the RSES (original version) as suggested by Tomas and Oliver (Tomas and Oliver, 1999). They also reported the same factor structure for the original version.

In present study, the validation of items construct was also performed by Rasch model. Rasch model is a mathematical model that follows modern response theory. Rasch model suggests that the probability of endorsing any response category to an item solely depends on the ability of the person ability and the difficulty of the item. This model uses log odd unit or logit scale that is considered as better and more accurate scale for analysing ordinal raw data including Likert scale (Baker, 2001). The output tables for fit statistics were generated by using Bond and Fox software*. Infit/outfit mean square values of each item were used to *verify the construct validity of each item. PTMEA* Corr values assessed the ability of each item to distinguish different level of abilities of respondents (Linacre 2002). All the items in RSES-M fitted the Rasch model and proved the construct validity of the translated scale that was consistent with the initial pilot study (Ahmad et al. 2016).

In order to achieve optimum control of asthma, pharmacist-led respiratory medication therapy ad-herence clinics (RMTAC) are introduced in healthcare system of Malaysia (Ahmad et al. 2015). The Malay version of study questionnaire can be administered to the patients at the time of their first visit to RMTAC. This will help the pharmacist to device the individualized patient-centred counselling and education.

4 CONCLUSION

The RSES-M proved to be a valid and reliable instrument for assessing SE of asthmatic patients and can be used to assess its association with other health outcomes. The RSES-M is psychometrically sound and appropriate to use as a screening tool and decision-aid in clinical settings to identify asthmatic patients who need more psychosocial support, counselling, and psychotherapeutic interventions such as cognitive behavioural therapy. Furthermore, the RSES-M can also be used for Malaysian patients living with other chronic illnesses to focus on psycho-social aspect influencing the successful management of the illnesses.

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Factors affecting mortality among patients undergoing hemodialysis in Sudan

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ABSTRACT: The study was aimed to determine factors affecting mortality among hemodialysis patients. This was a prospective observational study of adult hemodialysis patients from twelve centers in Khartoum from 1 August 2012 to 31 July 2013. A standardized data collection form was used in 1015 patients. Factors were evaluated using Cox regression. The analyzed patients were (534; 52.6%) and the excluded patients were; (194; 19.1%) transferred to other centers, (165; 16.3%) died, (84; 8.3%) lost to follow-up and (38; 3.7%) underwent renal transplantation. Age of '45–64' year [HR = 1.65, 95% CI (1.09–2.49)]; age '≥ 65', HR = 2.30, (1.46–3.62); hyperlipidemia, HR = 2.10, (1.33–3.32); diabetes mellitus, HR = 1.43, (1.02–1.99) and 'oral iron and vitamins' HR = 2.30, (1.51–3.51) were factors increase mortality. Female, HR = 0.55, (0.37–0.82); smoking, HR = 0.53, (0.36–0.79), and pyelonephritis, HR = 0.22, (0.05–0.88) were inversely associated. Advanced age, hyperlipidemia, diabetes mellitus and 'oral iron and vitamins' were important factors significantly affecting mortality.

1 INTRODUCTION

Anemia is a severe complication of end stage renal disease (ESRD). This is mostly due to erythropoietin deficiency, which contributes to higher rates of morbidity and mortality among hemodialysis (HD) patients (National Kidney Foundation 2002). It has been well documented that anemia is an indicator for lower survival rate in dialysis and pre-dialysis patients (Fort et al. 2010, Portolés et al. 2013, Rottembourg et al. 2013, Kwon et al. 2015). The annual mortality among HD patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS) was 21.7% in the US, 15.6% in Europe and 6.6% in Japan (Goodkin et al. 2003). However, in recent studies, it has ranged between 5.8%–19% (Malyszko et al. 2014, Rottembourget et al. 2015, Kaze et al. 2015).

Several studies conducted elsewhere have reported that at least one traditional cardiovascular disease (CVD) risk factor contributes to increased mortality risk in dialysis patients, including; patient race, advanced age, gender, smoking, and diabetes mellitus (DM) (Go et al. 2004, Shaza et al. 2005, Buargub 2008, Banerjee et al. 2009, Hanafusa et al. 2014). The factors affecting mortality among HD patients in Sudan are not well-known. This study aimed to determine the factors affecting mortality among anemic ESRD patients undergoing HD in Khartoum State.

2 METHODS

A prospective observational study was carried out with 1015 HD patients recruited from twelve stratified governmental HD centers in Khartoum State, Sudan. Patients over 18 years old and dialyzed at least 4 months from August 1, 2012, to July 31, 2013, and signed a written informed consent for participation thatwas included in the study. However, patients who had malignancy or rheumatoid arthritis were excluded from the study.

Patients were followed-up till lost to follow, renal transplantation, transfer to other centers, end of the study or death. In this study, anemia was defined, based on the (Kidney Disease: Improving Global Outcomes [KDIGO] Anemia Work Group 2012) definition, as hemoglobin (Hb) level <12 g/dL (<120 g/L) females and <13.0 g/dL (<130 g/L) in males, adult and children >15 years with chronic

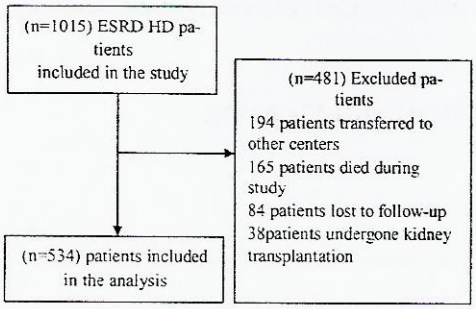

Figure 1. Flow chart of the study.

kidney disease (CKD). The patient registration records were used to identify patients at the HD centers. A standardized data collection form was used. Patient's information included socio-demographic such as age, sex, race, height and dry weight; social factors, including insurance status, education level, employment status, monthly income, and marital status were recorded, along with smoking and alcohol consumption. Patients' medical records were used for clinical data, including comorbidities, the etiology of ESRD and its duration, and laboratory data, as well as, data regarding anemia medications and other concurrent drugs.

The body mass index (BMI) was computed for each patient as weight in kilograms divided by the square of height in meters and categorized into five standard groups. The Modification of Diet in Renal Diseases (MDRD) equation was used for the estimation of glomerular filtration rates (eGFR) (Levey et al. 1999). The study protocol was approved by the National Center for Kidney Diseases and Surgery, Ministry of Health, Sudan and other approvals from the HD centers for recruiting of patients were obtained.

The Statistical Package for Social Sciences (SPSS) version 22.0.1 (SPSS 2013), was used for data analysis. The statistical significance of variables was taken as $p<0.05$. Categorical variables were presented as frequencies and percentages, and continuous variables were presented as means (±SD). The Cox proportional hazard regression models were used as univariate and backward stepwise adjusted multivariate methods to determine factors affecting mortality. More than two categorical variables were introduced as dummy variables. All independent variables were considered for inclusion in the multivariate models. A value of $p<0.05$ with mortality hazard ratio (HR) > 1 was considered as a significant factor.

3 RESULTS AND DISCUSSIONS

One thousand and fifteen patients were enrolled in the study. Four hundred and eighty-one patients were excluded due to 194 (19.1%) patients transfer to other centers, 165 (16.3%) mortality, 84 (8.3%) loss to follow and 38 (3.7%) underwent kidney transplantation. Five hundred and thirty-four patients (52.6%) were included in the analysis. The mean age of the included patients was 48.7 ± 16.1 years. The majority were males 307 (57.5%). The baseline characteristics of the study patients are illustrated in Table 1 and Table 2, respectively. All study patients were suffering from normochromic normocytic anemia. The mean baseline Hb level of

Table 1. Socio-demographic characteristics of HD patient (n = 534).

Variables	n (%)
Comorbidities	
Others diseases	67 (12.5)
Gout	55 (10.3)
No comorbid disease	47 (8.8)
Hyperlipidemia	21 (3.9)
Liver disease	10 (1.9)
Postoperative complication	7 (1.3)
Malnutrition	1 (0.2)
Etiology of ESRD	
Hypertension	297 (55.6)
Diabetes mellitus	135 (25.3)
Obstructive uropathy	79 (14.8)
Other causes	81 (15.2)
Treatment	40 (7.5)
Unknown	37 (6.9)
Chronic glomerulonephritis	37 (6.9)
Pyelonephritis	37 (6.9)
Intestinal nephropathy	6 (1.1)
Hereditary nephropathy	3 (0.6)
Duration of hypertension (years)	
No hypertension	237 (44.4)
≤3	39 (7.3)
>3–6	69 (12.9)
>6–9	48 (9.0)
>9	141 (26.4)
Duration of diabetes mellitus (years)	
No Diabetes mellitus	399 (74.7)
≤5	18 (3.4)
>5–10	39 (7.3)
>10–15	31 (5.8)
>15–20	25 (4.7)
>20	22 (4.1)
Anemia medication	
ESA + IV iron + oral iron + vitamins	211 (39.5)
IV iron + oral iron + vitamins	159 (29.8)
ESA + IV iron + vitamins	77 (14.4)
Oral iron + vitamins	32 (6.0)
ESA + oral iron + vitamins	32 (6.0)
IV iron + vitamins	18 (3.4)
ESA + vitamins	5 (0.9)

ESA: Erythropoiesis-stimulating agent.

Table 2. Prognostic factors of anemia mortality hazard from simple Cox regression analysis.

Variables	Unadjusted HR (95% CI)	*p*-value
Female vs. male	0.86 (0.63, 1.18)	0.346
Sudanese vs. others	0.05 (0.00, 67.28)	0.413
Age groups		
18–44 (years) (Ref)	0	
45–64	1.70 (1.14, 2.54)	0.009
≥65	2.99 (1.99, 4.51)	<0.001
BMI (kg/m²)		
Underweight <18.5 (Ref)	0	
Normal weight 18.5–24.9	0.79 (0.56, 1.11)	0.170
Overweight ≥25	0.51 (0.16, 1.65)	0.262
≥secondary school vs. Secondary	1.18 (0.86, 1.62)	0.297
Uninsured vs. Insured	1.07 (0.79, 1.46)	0.662
Nonsmoker vs. Smoker	0.80 (0.58, 1.10)	0.165
Non-alcoholic vs. Alcoholic	1.21 (0.84, 1.75)	0.299
Family history of ESRD (no/yes)	1.47 (1.03, 2.11)	0.033
Comorbidities		
No comorbid disease (no/yes)	0.59 (0.30, 1.15)	0.119
Liver disease (no/yes)	1.63 (0.72, 3.67)	0.243
Hyperlipidemia (no/yes)	2.78 (1.78, 4.32)	<0.001
Gout (no/yes)	1.22 (0.77, 1.93)	0.396
Others (no/yes)	0.84 (0.52, 1.37)	0.492
Etiology of ESRD		
Hypertension (no/yes)	1.56 (1.13, 2.15)	0.007
Diabetes mellitus (no/yes)	1.93 (1.41, 2.62)	<0.001
Glomerulonephritis (no/yes)	1.25 (0.72, 2.15)	0.431
Obstructive uropathy (no/yes)	0.81 (0.51, 1.29)	0.378
Pyelonephritis (no/yes)	0.20 (0.05, 0.80)	0.023
Interstitial nephropathy (no/yes)	0.98 (0.24, 3.96)	0.989
Treatment (no/yes)	0.43 (0.18, 1.05)	0.065
Others (no/yes)	0.69 (0.41, 1.16)	0.164
Unknown (no/yes)	0.73 (0.38, 1.38)	0.327
Duration of hypertension/years		
≤3 (Ref)	1	
>3–6	1.47 (0.92, 2.37)	0.111
>6–9	1.11 (0.60, 2.06)	0.733
>9	1.82 (1.29, 2.56)	0.001
Duration of DM/years		
≤5 (Ref)	0	
>5–10	1.63 (0.96, 2.77)	0.068
>10–15	1.99 (1.18, 3.38)	0.010
>15–20	2.15 (1.27, 3.65)	0.004
>20	2.49 (1.47, 4.22)	0.001
Anemia medications		
IV iron + oral iron + vitamins (Ref)	1	
Oral iron + vitamins	2.15 (1.34, 3.44)	0.001
IV iron + vitamins	0.78 (0.28, 2.17)	0.638
ESA + vitamins	1.25 (0.30, 5.13)	0.758
ESA + IV iron + oral iron + vitamins	0.89 (0.61, 1.29)	0.544
ESA + IV Iron + vitamin	0.77 (0.45, 1.33)	0.348
ESA + oral iron + vitamin	0.57 (0.25, 1.33)	0.195

BMI: Body mass index: DM; Diabetes mellitus: Ref; Reference.

included patients was 7.89 ± 1.24 g/dL. It was 9.37 ± 0.96 g/dL at the end of follow-up. Sixty-seven percent of patients had Hb < 10 g/dL. Only 144 (27%) patients were diagnosed for iron status [ferritin and transferrin saturation (TSAT)].

In this study, the mortality rate among HD patients was 16.3%. This result is similar to the findings of the DOPPS study from Euro-DOPPS countries of 1-year mortality rate in Germany; however, it was lower than the findings in UK 18.6% (Rayner et al. 2004). Moreover, it was greater than the findings in ESRD HD patients in France (13.8%) (Rottembourg et al. 2015). In the current study the results of simple (Table 2) and multiple (Table 3).

Table 3. Prognostic factors of anemia mortality hazard from multiple Cox regression analysis.

Variables	Adjusted HR (95% CI)	
	Model*	Model*
Gender		
Male	1	1
Female	0.54 (0.36, 0.81)[b]	0.55 (0.37, 0.82)[b]
Age groups		
18–44	1	1
45–64	1.69 (1.12, 2.56)[a]	1.65 (1.09, 2.49)[a]
≥65	2.40 (1.52, 3.78)[c]	2.30 (1.46, 3.62)[c]
Smoking habit		
Non smoker	1	1
Smoker	0.54 (0.36, 0.80)[b]	0.53 (0.36, 0.79)[b]
Hyperlipidemia		
No	1	1
Yes	1.92 (1.21, 3.06)[b]	2.10 (1.33, 3.32)[b]
Diabetes mellitus		
No	1	1
Yes	1.43 (1.02, 2.00)[a]	1.43 (1.02, 1.99)[a]
Pyelonephritis		
No	1	0
Yes	0.21 (0.05, 0.84)[a]	0.22 (0.05, 0.88)[a]
Anemia medications		
IV iron + oral iron + vit	1	1
Oral iron + Vit	2.41 (1.58, 3.68)[c]	2.30 (1.51, 3.51)[c]

[a]P <0.05; [b]P <0.01; [c]P <0.001; Vit: vitamin B_{12} and/or folic acid.

*Model adjusted with all socio-demographic and clinical variables;

*Model adjusted for variables: Gender, age, smoking, hyperlipidemia, diabetes mellitus, and pyelonephritis and anemia medication.

Cox regression analysis that the significant prognostic factors of anemia mortality hazard among HD patients, including patients' age '45–64' years (HR = 1.65), age '≥ 65' years (HR = 2.30), DM (HR = 1.43), hyperlipidemia (HR = 2.10), and combination of 'oral iron and vitamins' (HR = 2.30). The factors which decreased the risk of mortality were female gender (HR = 0.55), smoking (HR = 0.53), and pyelonephritis (HR = 0.22), as presented in (Table 3).

This study found that hyperlipidemia was the factor associated with higher mortality risk in HD patients. Conversely, the previous study documented that hyperlipidemia decreases the odds to associated with the 2-year mortality rate in HD (Fleischmann et al. 2001). The predominance of other traditional risk factors such as advanced age, hypertension, DM, and obesity, in addition to, uremia-relating factors including; inflammation, anemia, oxidative stress, coronary calcification and hyperphosphatemia, may explain this discrepancy.

Consequently, the systemic inflammation and malnutrition may contribute to the inverse correlation between cholesterol levels and mortality by cholesterol-lowering effects (Liu et al. 2004). However, malnutrition has increased levels of C reactive protein (CRP), interleukin-6 (IL-6) and concomitant CVD in a dialysis patient, and others diseases cause ESRD. Therefore, CKD may contribute directly to the inflammation-malnutrition-atherosclerosis (MIA) paradigm (Kaysen and Eiserich 2004). Concurrent of malnutrition and inflammation in HD patients may modify the relationship between cholesterol and CVD, as well as mortality. However, in the general population, the pathophysiology and the spectrum of CVD may differ from dialysis patients. Notably, HD patients may experience atherosclerosis, cardiac dysfunction and sudden cardiac death from arrhythmia (Qunibi 2015).

The present study has shown that DM was the most important factor which increased mortality risk among HD patients. This result was in agreement with results which showed that DM increased mortality hazard among dialysis patients (Rayner et al. 2004). Moreover, diabetic nephropathy was associated with higher mortality risk in dialysis patients (Wallen et al. 2001, Remppis and Ritz 2008, Banerjee et al. 2009, März et al. 2011). This may explain the association between lower baseline Hb level and the progression to ESRD (Mohanram et al. 2004), leading to CVD complications. Conversely, DM was found to be decreased mortality risks in HD patients with CVD or atherosclerosis and anemia (Maekawa et al. 2008). However, according to Besarab et al. (1998), DM was not associated with mortality related to non-fatal myocardial infarction among cardiac HD patients with and without normal Hct level.

This study revealed that drug pattern of 'oral iron and vitamins' is associated with higher mortality risk. Patients receiving this combination, without IV iron and erythropoiesis-stimulating agents (ESAs), may experience anemia with higher rates of complications and death. These findings consistent with the results of the previous study which showed that higher Hb levels inversely associated with mortality risk among HD patients (Roberts et al. 2006), thus, confirming that decreased mortality risks were associated with increased epoetin requirements (Xue et al. 2002). Concomitant use of iron supplements and ESAs is required for erythropoiesis and complete anemia management in HD patients (Tsubakihara et al. 2010). In contrast, the Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHIOR) and Cardiovascular Risk Reduction by Early Anemia Treatment (CREAT) randomized control trials (RCT) in pre-dialysis and dialysis CKD patients, respectively, documented that management of anemia with epoetinalfa was associated with higher mortality risk related to CVD complications without improving the patients' quality of life in comparison to patients with lower Hb levels (Singh et al. 2006, Drüeke et al. 2006). These variations may be due to differences in study designs and populations.

This study showed that the female gender is negatively associated with the risk of death among study patients. Conversely, the female was associated with a higher risk of mortality of all-causes among HD patients (Stidley et al. 2006). This is consistent with previous studies which found that male patient positively associated with risk of mortality (Rayner et al. 2004, Furth et al. 1998, Bloembergen et al. 1994). The findings of this study are, in agreement with Libyan study which found that diabetic HD men associated with higher mortality risk than diabetic HD women (Buargub 2008). Consistently, male gender was found as a prognostic factor for mortality among HD patients in Sudan (Elamin and Abu-Aisha 2012). The ethnic and racial differences, variation in the definition of anemia and Hb cut-offs, and the higher frequency of comorbidities and conventional risk factors in different geographical regions. All these reasons may explain the disparities of these results.

The current study has revealed an inverse association between smoking and mortality risks among HD patients. However, this was not supported by previous data (Furth et al. 1998, Suskin et al. 2001, Fleischmann et al. 2001, Whelton et al. 2002, Banerjee et al. 2009), as well as the reality, that smoking was considered as an important remarkable factor which had negative effect on kidney function (Orth 2004). In contrast, higher mortality risk was reported among smoker diabetic HD patients than non-smoker counterpart (Buargub 2008). Inconsistent with the findings of this research was, the Medicare claims data study by the U.S Renal Data System (USRDS) Wave 2 cohort, which found that smoker dialysis patients were at higher risk of mortality related CVD causes (Foley et al. 2003). This variation can only be explained due to the fact that in this study the data revealed more than fifty percent of patients were non-smokers.

Furthermore, the present study has found that pyelonephritis was a factor which significantly decreased the risk of death among HD patients. Due to the lack of data regarding the association of pyelonephritis with mortality among HD patients, however, these results were inconsistent with a study found that in general population both men and women had a higher risk of death if they had not been hospitalized for acute pyelonephritis (Foxman et al. 2003). Conversely, pyelonephritis was known as a cause of mortality among both genders in South Korean (Ki et al. 2004). This might be related to the increased rates of pyelonephritis associated renal and infectious diseases.

The limitations of this study need to be mentioned. The presence of death as a major serious clinical outcome was recorded from patient medical records. However, causes of death were not reported as they were sometimes unknown or unavailable.

4 CONCLUSIONS

The current research has shown that older patients, patients with hyperlipidemia, DM, and receiving drug combination of 'oral iron and vitamins' were more likely to have a greater risk of mortality. However, females, smokers, and patients with pyelonephritis were negatively associated with mortality in this research. This study highlighted the necessity to early recognition and control of the risk factors that affecting mortality among ESRD HD patients, as well as, to decrease mortality rate, the burden of anemia management, and improve patient's quality of life.

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Evaluating the effectiveness of filgrastim in patients with solid cancer

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ABSTRACT: Neutropenia caused by chemotherapy may delay treatment and reduce the therapeutic outcome. The objective of this study was to determine the difference in Absolute Neutrophil Count (ANC) recovery time between filgrastim brand name A and brand name B in patients with solid cancer at Dr. Sardjito Hospital, Yogyakarta, Indonesia. Data were obtained on the basis of the number of episodes of neutropenia. The result indicated an increased difference in ANC recovery time between filgrastim A administration at a dose of 6544.95 ± 6041.64/mm^3 and filgrastim B administration at a dose of 7521.54 ± 7008.15/mm^3. Through the survival analysis using the Kaplan–Meier curve, we revealed that there was no significant difference between the two types of filgrastim in achieving ANC recovery ($p > 0.05$). The results of the chi-square test indicated a significant difference between the grade of neutropenia and the time to achieve ANC recovery ($p < 0.05$). There was no statistically significant difference in the time required to achieve ANC recovery time between the brand names filgrastim A and filgrastim B.

1 INTRODUCTION

1.1 *Background*

Neutropenia after chemotherapy may prolong hospital stay as well as increase the risk of infection; furthermore, it will also require delays and reduction of doses for chemotherapy (Crawford et al. 2003). Neutropenia may occur without fever that is defined as the number of ANC <1000/mm^3 and may decrease to <500/mm^3 for 48 h (Alberta Health Services 2014, NCCN 2013). According to Common Terminology Criteria for Adverse Events (CTCAE), chemotherapy-induced neutropenia is classified into grades 1–4: grade 1 is ANC <2000–1500/mm^3, grade 2 is ANC <1500–1000/mm^3, grade 3 is ANC <1000–500/mm^3, and grade 4 is ANC <500/mm^3 (NCI 2009, 2006). Approximately 20–40% neutropenia occurs in solid cancers (Bolis et al. 2013). The use of myelosuppressive agents such as doxorubicin, docetaxel, cyclophosphamide, 5-FU, leucovorin, irinotecan, oxaliplatin, and etoposide poses risk for the occurrence of neutropenia (Lyman et al. 2014, Weycker et al. 2014).

Filgrastim is one of the hematopoietic growth-stimulating factors such as cytokines that regulates the proliferation, differentiation, and function of hematopoietic cells (Schouten 2006). Several clinical trials and meta-analyses have demonstrated significant reduction in the risk of febrile neutropenia in patients who received *granulocyte colony-stimulating factor* as primary prophylaxis after chemotherapy (Aapro et al. 2011). Studies on new similar products have compared the effects XM02 and Neupogen™ in patients with breast cancer during the first cycle. The results indicated that the average time required for ANC recovery was 8.0 days for XM02, 7.8 days for Neupogen™, and 14 days for placebo (Del Giglio et al. 2008).

It proves that medicinal products containing the same active ingredients have the same activity. Two bioequivalent products show the same bioavailability and are thus expected to provide the same therapeutic effect (Peterson 2011).

In fact, on the basis of the observation of clinicians, some cases in the elderly with breast cancer in Dr. Sardjito Hospital showed that filgrastim A results in longer recovery, which required larger doses or a vial when compared with filgrastim B. Therefore, it is necessary to conduct an evaluation to improve the quality of health services. Changes made to the manufacturing process will obviously reflect in the products. Chemical synthetic drugs have qualitative and quantitative compositions similar to the original product, whereas biosimilar products were produced from the synthesis of a living

cell. As a result, biosimilar products may not have the same composition and pharmacological mechanism as the reference product (Haustein 2012).

1.2 *Research objective*

The objective of this study was to determine the difference in ANC recovery time between the brand names filgrastim A and filgrastim B in patients with solid cancer at Dr. Sardjito Public Hospital.

2 METHODS

2.1 *Type and research design*

This was a non-experimental study with retrospective cohort design. The data were taken from the medical records during January 2013 to March 2015 of patients with solid cancer who underwent therapy with filgrastim at Dr. Sardjito Hospital, Yogyakarta, Indonesia.

2.2 *Ethical approval*

Approval of the study was obtained from the local institutions where the study was conducted. In addition, the study received ethical approval from Faculty of Medicine, Universitas Gadjah Mada with issued Ref: KE/FK/166/EC.

2.3 *Patients*

The study population constituted patients with solid cancer who also had neutropenia and underwent filgrastim therapy. Inclusion criteria for this study were patients with solid cancers, age >18 years, neutropenia with an ANC <1500/mm^3, received filgrastim A or B as a therapy with or without antibiotic therapy, and had complete laboratory data had regarding leukocyte and neutrophil counts in each cycle.

Exclusion criteria for this study were patients who were diagnosed with hematologic malignancies and cancer and received radiotherapy and filgrastim therapy but did not have complete data on leukocyte and neutrophil counts in each cycle.

A total of 146 neutropenia episodes met the inclusion criteria, including 76 samples in the filgrastim A group and 70 samples in the filgrastim B group.

3 RESULTS AND DISCUSSION

3.1 *Data collection process of the study subjects*

Data were collected from medical records (inpatient) and Tulip integrated cancer department (outpatient) at Dr. Sardjito Hospital, which were then verified by the pharmacy department, the information technology department, and clinical laboratory department.

This study included 338 patients with solid cancer who experienced neutropenia after chemotherapy. However, only 97 patients with 146 episodes of neutropenia met the inclusion criteria. The data were processed on the basis of episodes of neutropenia, that was, the occurrence of neutropenia in each cycle of chemotherapy.

3.2 *Characteristics of the study subjects*

The observed data characteristics of the study population were gender, age, body mass index (BMI), type of solid cancer, type of cancer drug regimens, chemotherapy cycles, episodes of neutropenia, grade of neutropenia, type and dose of filgrastim.

According to this study, women were more likely to have neutropenia than men, as shown in the distribution of episodes based on gender (female 80.1%). Previous studies have shown that gender was one of the risk factors for neutropenia (Crawford et al. 2005, Lyman et al. 2014). In addition, research results on the management of febrile neutropenia stated that being female was a risk factor and determinant of prognosis of febrile neutropenia (Alberta Health Services 2014, Lyman et al. 2003).

The overall incidence of neutropenia in patients >50 years of age was 66.4%, whereas it was 33.6% for patients <50 years of age. Another study has shown that the age >65 years was a risk factor for the occurrence of neutropenia in patients with cancer who receive chemotherapy (Aapro et al. 2006) because of the fact that the function of immune system decreases with aging (Aspinall 2005). The average age of patient experiencing grade 1–2 neutropenia was 49 years, whereas for grade 3–4 neutropenia, it was 56 years (Doshi et al. 2012).

Average patients had normal BMI at 69.2%. Low BMI can increase the risk of febrile neutropenia (Chan et al. 2012). Another study reported that nutritional factors and inflammation increased the toxicity of chemotherapy (Alexandre 2003), whereas obese patients were unlikely to experience hematologic toxicity or delays of chemotherapy cycle due to myelosuppression (Peter et al. 2007, Pettengell et al. 2008).

This study showed breast cancer as the most common condition of neutropenia (41.1%), followed by colorectal cancer (13.0%), cervical cancer (8.9%), ovarian cancer (7.5%), and endometrial cancer and lung cancer (4.1%). Factors related to disease, such as type of tumor, is a predictor of febrile neutropenia, for example, febrile neutropenia often occurs in solid cancer such as breast cancer, lung cancer, colorectal cancer, and ovarian cancer (Lyman et al. 2011).

The result indicated that in the patient group with breast cancer who underwent *alkylating-anthra-*

cyclines chemotherapy (doxorubicin–cyclophospamide), *anthracyclines-taxanes* (doxorubicin–paclitaxel), docetaxel, and *antimetabolite-platinum* group (gemicitabine–carboplatin), the value of ANC was lowered to grade 3–4. Similar results were obtained in some types of chemotherapy regimens in nasopharyngeal cancer, such as *taxanes-platinum* (paclitaxel-carboplatin) and *platinum-antimetabolite* (cisplatin–5FU), and in colon cancer using *avastin-leucovorin–5FU* and *folfiri*.

Chemotherapy regimen is one of the factors initiating side effects such as neutropenia. This condition is also influenced by the patient's genetic polymorphism affecting cancer drug metabolism (Efferth & Volm, 2005, Petros et al. 2005). The study conducted by Hurria et al. and Lyman et al. showed that the chemotherapeutic group of anthracyclines, taxanes, and alkylators were myelosuppressive agents that can decrease the value of the ANC (Hurria et al. 2005, Lyman et al. 2014).

Neutropenia may delay the time of chemotherapy in the next cycle. The average episode of neutropenia in patients with solid cancers in this study occurred only once in each cycle. In this study, the highest incidence of neutropenia occurred in the third cycle (21.9%), followed by the first cycle (20.5%) and the second cycle (19.2%). This is not in accordance with some previous studies, which stated that the incidence of neutropenia in solid cancers occurred in the first cycle (Anonymous 2010, Crawford et al. 2008). This difference was probably due to the daily clinical practice in Dr. Sardjito Public Hospital of using filgrastim not as prophylaxis but as a supportive therapy in the management of neutropenia. According to Carr, one of the indications for the use of G-CSF is as a primary and secondary prophylaxis (Carr 2012).

Research conducted by Schwenkglenks et al. stated that the occurrence of neutropenia in the first cycle may act as the predictor for the occurrence of neutropenia in the next cycle (Schwenkglenks et al. 2006). Prophylactic G-CSF may reduce the risk of chemotherapy-induced neutropenia and recommended in patients receiving chemotherapy regimen that has a high risk of febrile neutropenia (Aapro et al. 2011).

In this study, both filgrastim A and filgrastim B had the same doses (300 µg) per vial. The number of vials used depended on the value of ANC observed, until it reached >1500/mm^3, and chemotherapy can be resumed. The results indicated that a dose of 300 µg/day (78.8%) and cumulative doses of 600 mg (13.7%), 900 µg (2.7%), and 1200 µg (4.8%) were required.

3.3 *Evaluating the effectiveness of filgrastim brand names A and B*

In this study, the effectiveness of filgrastim was assessed from the time to ANC recovery, on the basis of the value of ANC recovery >1500/mm^3. Wilcoxon test results for the difference in ANC before and after the administration of filgrastim brand names A and B showed $p < 0.05$ (0.000). This indicates that both filgrastim brand names A and B can increase the value of the ANC. The results of the paired sample t-test analysis of the increase in ANC before and after the administration of filgrastim brand names A and B are summarized in Table 1.

The results of the independent sample t-test analysis of the difference in ANC between filgrastim brand names A and B are summarized in Table 2.

The *independent sample t-test* showed that the average value of the increased difference in ANC in filgrastim brand name B was greater than that in filgrastim brand name A, but the statistical test showed $p > 0.05$ (0.278), which means that there was no significant difference in the increase of ANC between filgrastim brand names A and B. Recovery or no recovery is determined by the value of ANC recovery, which is classified as recovery if ANC >1.500/mm^3. This figure is used in accordance with the treatment standard in Dr. Sardjito Public Hospital (Ministry of Health, 2013).

The result indicated that recovery was <6.16%, when compared with 93.84%, which indicates that filgrastim can be used in the therapy of neutropenia. This is in accordance with that of indications for using G-CSF as a supportive therapy (Carr, 2012). The Kaplan–Meier curve of the type of filgrastim with ANC recovery time (day) is shown in Figure 1.

The survival test results for the difference in time to achieve ANC recovery between filgrastim brand

Table 1. Difference in ANC recovery time before and after filgrastim administration.

Group	Mean ± SD (/mm^3)	P
ANC before filgrastim A administration	893.66 ± 421.58	*0.000
ANC after filgrastim A administration	7438.62 ± 6225.96	
ANC before filgrastim B administration	673.34 ± 455.18	*0.000
ANC after filgrastim B administration	8194.88 ± 7142.39	

Table 2. Results of the difference in ANC between filgrastim brand names A and B.

Group	Mean ± SD (/mm^3)	P
Filgrastim A	6544.95 ± 6041.64	0.278
Filgrastim B	7521.54 ± 7008.15	

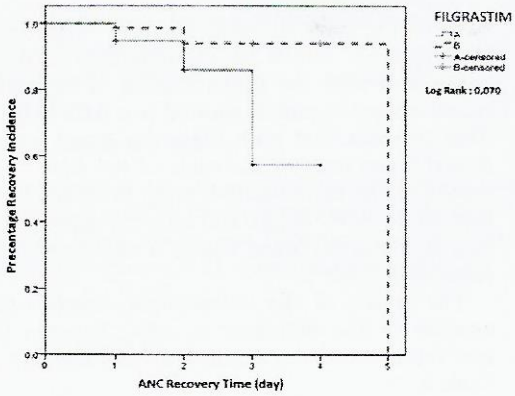

Figure 1. Kaplan–Meier curve of filgrastim type with ANC recovery time.

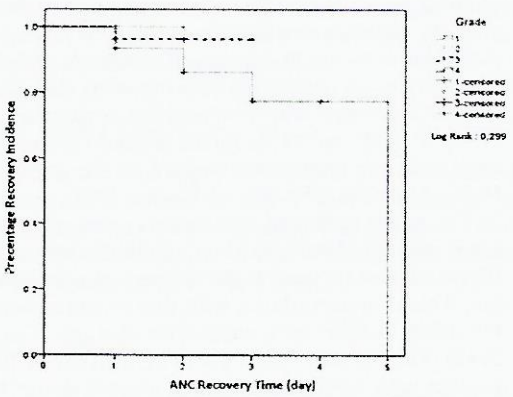

Figure 2. Kaplan–Meier curves of the neutropenia grade with ANC recovery time.

names A and B showed $p > 0.05$ (0.070), which indicates no significant difference between the two types of filgrastim in achieving ANC recovery. The Kaplan–Meier curve based on the grade of neutropenia with ANC recovery time is shown in Figure 2.

The Kaplan–Meier curves of the neutropenia grade with ANC recovery time (Figure 2) shows that the higher the grade of neutropenia, the longer the time needed to reach ANC recovery. Table 3 presents the result of the chi-square test between independent and confounding variables with recovery time.

It is evident from Table 3 that the grade of neutropenia could affect recovery time ($p < 0.05$). The results of the chi-square test indicate that the higher the grade of neutropenia, the longer the duration of neutropenia and the recovery time. There is no significant difference between the two types of filgrastim in achieving ANC recovery time. Biosimilar products show equality in pharmacokinetics,

Table 3. Results of the chi-square test between independent and confounding variables with recovery time.

Description	P
Sex vs recovery time	0,123
Age vs recovery time	0,936
Body mass index vs recovery time	0,829
Cycle vs recovery time	0,969
Neutropenia episode vs recovery time	0,521
Neutropenia grade vs recovery time	0,015*
Filgrastim type vs recovery time	0,365
Cumulative dose vs recovery time	0,324
Regimen type vs recovery time	0,843
Cancer type vs recovery	0,368

*Results indicate significant difference.

pharmacodynamics, and safety profile, as well as in the effectiveness (Aapro 2013). Gascon reported that filgrastim biosimilar to Nivestim when compared with Neupogen™ produced therapeutic equivalence between the two products in terms of average ANC nadir value and ANC recovery time (Gascon 2012).

4 CONCLUSION

This study concluded that there was no statistically significant difference in ANC recovery time between filgrastim brand names A and B.

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