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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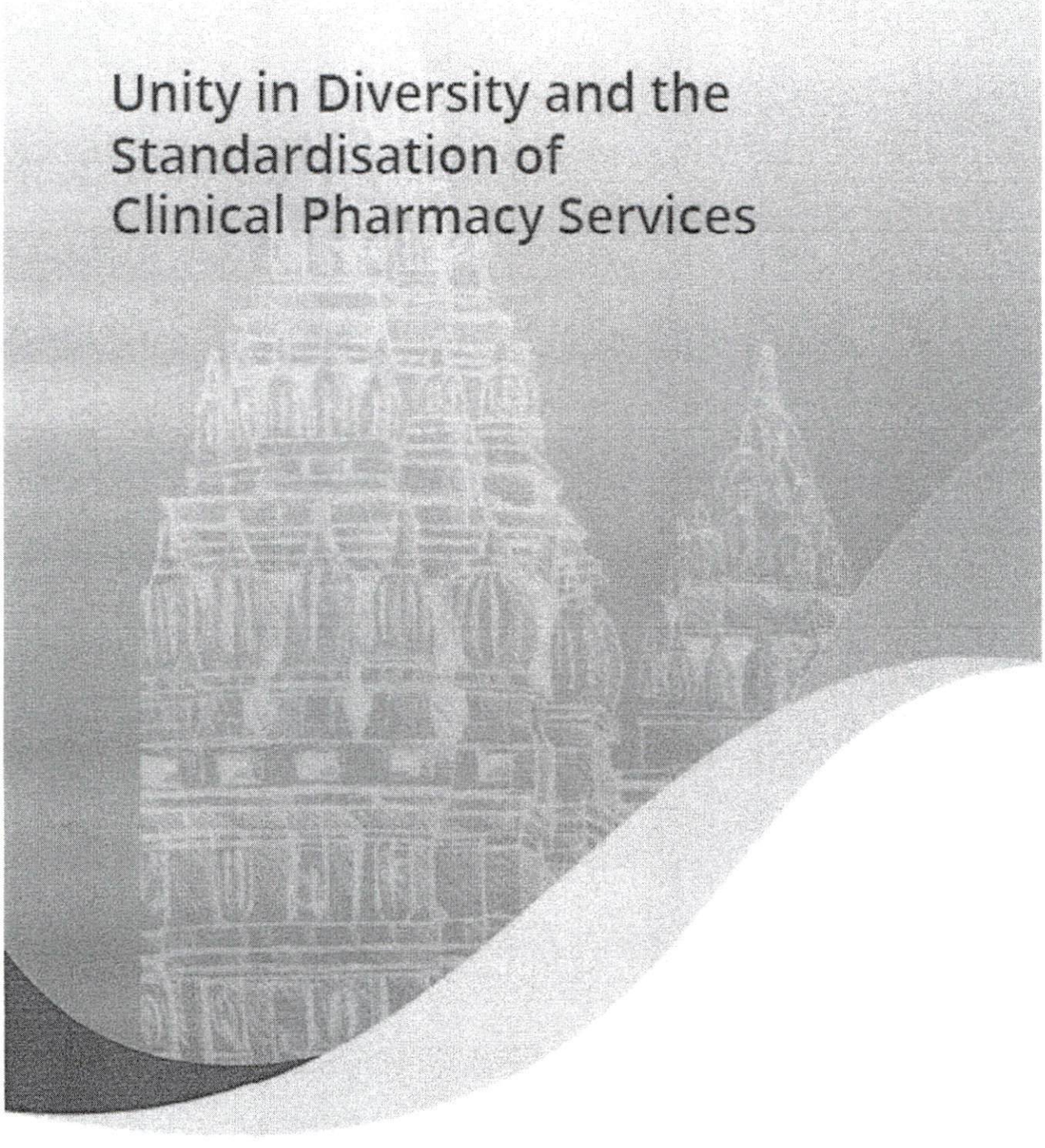

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UNITY IN DIVERSITY AND THE STANDARDISATION OF CLINICAL PHARMACY SERVICES

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Unity in Diversity and the Standardisation of Clinical Pharmacy Services

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Table of contents

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.

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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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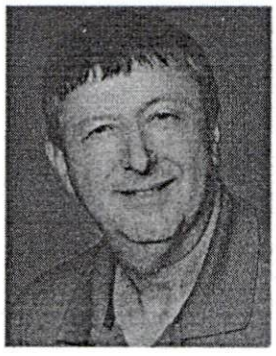
Plenary speakers

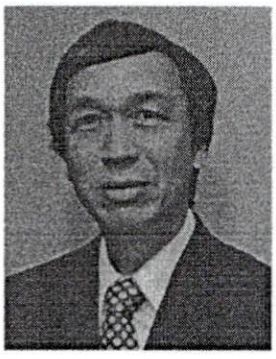


Prof. Michael D. Katz—*Professor at Department of Pharmacy Practice & Science, The University of Arizona College of Pharmacy, USA*

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

Dr. Hiroyuki Kamei—*Office of Clinical Pharmacy Practice and Health Care Management, Faculty of Pharmacy, Meijo University, Nagoya, Japan*
Dr. Hanna Sung—*University of the Pacific, Thomas J. Long, School of Pharmacy and Health Sciences in California, USA*
Dr. Alexandre Chan—*Deputy Head and a tenured Associate Professor at the Department of Pharmacy, Faculty of Science at National University of Singapore (NUS) and the Duke-NUS Medical School, Singapore*
Prof. Jae Wook Yang—*Professor and Director of the Institute of Clinical Research and Practice, College of Pharmacy, Sahhmyook University & Vice President of Korean College of Clinical Pharmacy*
Prof. Dr. Syed Azhar Syed Sulaiman—*Professor at School of Pharmaceutical Sciences at University Sains Malaysia, Penang, Malaysia*

SYMPOSIUM 3: MOLECULAR PHARMACOLOGY AND PHARMACOGENOMICS

Dr. Mehdi Rajabi—*Clinical Pharmacy and Pharmacy Practice, Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran. Clinical Pharmacist, Member of General Pharmaceutical Council of Great Britain*
Mrs. Fan Zhang—*Lanzhou University, a Pharmacist-in-Charge at Pharmacy Department of the First Hospital of Lanzhou University in China*
Dr. Lunawati Bennet—*Assoc. Professor of Pharmaceutical Sciences at Union University School of Pharmacy in Jackson, Tennesse, USA*
Prof. Robert D. Sindelar—*Professor and former Dean of Faculty of Pharmaceutical Sciences, University of British Columbia; and Advisor, External relations, Centre for Health Evaluation & Outcomes Sciences (CHEOS), Providence Health Care research Institute and University of British Columbia, Canada*
Dr. Baharudin Ibrahim—*School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia*

SYMPOSIUM 4: INTERPROFESSIONAL EDUCATION

Dr. Christine B. Teng—*Assoc. Professor of Department of Pharmacy, National University of Singapore Principal Pharmacist (Clinical), Dept of Pharmacy, Tan Tock Seng Hospital, Singapore*
Mr. Tan Wee Jin—*Principle Pharmacist at Guardian Health & Beauty, Singapore*
Dr. Ching Jou Lim—*Senior lecturer in the Discipline of Social and Administrative Pharmacy, University Sains Malaysia, Malaysia*
Mr. Mac Ardy J. Gloria—*University of the Philippines, The Philippines*
Dr. Vivian Lee Wing Yan—*Assoc. Professor of the School of Pharmacy and the Assistant Dean (Student Development) of the Faculty of Medicine, Chinese University of Hong Kong*

SYMPOSIUM 5: ADVANCED PRACTICE 2

Prof. Timothy E. Welty—*Professor and Chair of Clinical Science in the College of Pharmacy and Health Sciences at Drake University, Iowa, USA*
Dr. Takao Shimazoe—*Department of Clinical Pharmacy and Pharmaceutical Care, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan*
Prof. Zhou Quan—*Professor and Vice Dean of Department of Pharmacy, The Second Affiliated Hospital of Zhejiang University, China*
Prof. Sukhyang Lee—*Professor of Clinical Pharmacy at College of Pharmacy, Ajou University, Korea*
Prof. Kheirollah Gholami—*Professor and Chairman at the Department of Clinical Pharmacy, College of Pharmacy, Iran*

SYMPOSIUM 6: HEALTH CARE DELIVERY IN COMMUNITY PHARMACY

Prof. Michael D. Hogue—*Assoc. Dean for the Center for faith and Health at Samford University's College of Health Sciences, Birmingham, Alabama, USA*
Dr. Elida Zairina—*Senior lecturer of Department of Pharmacy Practice, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia*
Ms. Leonila M. Ocampo—*Chairman of the Hygieian Insitute for Education, research and Training Inc, The Philippines*
Ms. Yong Pei Chean—*Senior Manager, Khoon Teck Puat Hospital and Council Member, Pharmaceutical Society of Singapore*
Drs. Saleh Rustandi—*Chairman of Himpunan Seminat Farmasi Masyarakat (HISFARMA) of Indonesia*

SYMPOSIUM 7: PHARMACY EDUCATION

Dr. Takashi Egawa—*Clinical Pharmaceutics and Health Sciences, Department of Pharmaceutical and Health Care Management, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka, Japan*
Prof. Yolanda R. Robles—*Professor and former Dean College of Pharmacy, University of the Philippines*
Prof. Rong-sheng Zhao—*Professor in Peking University Third Hospital, China. Assistant to President, Deputy-Director in Pharmacy Department of Peking University Third Hospital, China*
Dr. Manit Saetewa—*Staff of Faculty of Pharmaceutical Sciences, Ubon Ratchathani University, Thailand*
Drs. Nurul Falah Eddy Pariang—*President of Indonesian Pharmacist Association, Indonesia*
Prof. Josepp T. Dipiro—*Dean, Professor and Archie O. McCalley Chair at the Virginia Commonwealth University, School of Pharmacy, Richmond, Virginia, USA*

SYMPOSIUM 8: ADVANCED PRACTICE 3

Dr. Daraporn Rungprai—*Academic Staff of Faculty of Pharmacy, Silpakorn University, Thailand*
Ms. Hong Yen NG—*President, 110th Council, Pharmaceutical Society of Singapore Specialist Pharmacist (Oncology), Singapore General Hospital*
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Dr. Junaidi Khotib—*Assoc. Professor of Department of Clinical Pharmacy at Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia*

SYMPOSIUM 9: IMPROVING PATIENT MEDICATION SAFETY

Dr. Wimon Anansakunwatt—*Siriraj Hospital, Thailand*

Mr. Mohammed Nazri Abdul Ghani—*Principal Pharmacist and Medication Safety Officer (MSO) of KK Women's & Children Hospital, Singapore*

Ms. Yoon Sook Cho—*Director of Pharmacy Department, Seoul National University Hospital, Korea*

Dr. Sutthiporn Pattharachayakul—*Assistant Professor at the Department of Clinical Pharmacy, Prince of Songkla University, Thailand*

Dra Mariyatul Qibtiyah—*Head of Paediatric Pharmacy Services at Dr Soetomo Hospital, Surabaya, Indonesia*

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The effect of Telmisartan on lipid levels and proinflammatory cytokines in ESRD patients undergoing hemodialysis

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ABSTRACT: Telmisartan acts as a partial selective agonist of PPARγ, thus might affect lipid and carbohydrate metabolisms. This study aimed to investigate the effect of Telmisartan on lipid profiles and Proinflammatory Cytokine (CRP) in ESRD patients. An observational study was conducted on ESRD patients with regular hemodialysis at least twice a week during the last three months, blood pressure predialytic >140/90 mmHg, and not using Telmisartan. Sixteen subjects were involved (12 male and four female). Pre-study levels of cholesterol, TG, HDL and LDL were normal. After three months of treatment with Telmisartan, the levels of cholesterol, TG, HDL and LDL were 127.31 mg/dl, 74 mg/dl, 50.06 mg/dl and 74.56 mg/dl, respectively, showing a decrease in lipid levels except for cholesterol. The level of CRP was slightly decreased after Telmisartan treatment from 0.47 ± 0.47 mg/dl to 0.34 ± 0.33 mg/dl. Thus, Telmisartan has a promising effect on decreasing lipid and cytokine proinflammatory levels in ESRD patients with hemodialysis.

1 INTRODUCTION

Increasing prevalence of end stage renal disease (ESRD) highly contributes to the cardiovascular complication event (47%) (Pernefri 2012). One of the comorbid conditions that play an important role in causing cardiovascular complication in ESRD is hypertension. On the other hand, the activation of renin angiotensin aldosterone system (RAAS) and insulin resistance through proinflammatory cytokines (IL-1, IL-6, TNF-α, etc), visceral adipose tissue, adipokines metabolism dysregulation (leptin, adiponectin, resistin), metabolic acidosis, hyperparathyroidism, anemia, other oxidative stress factors and uremia toxin are also responsible for cardiovascular complications (Hung & Ikizler, 2011).

There are several pharmacological agents that have been developed to reduce insulin resistance by increasing insulin sensitivity, e.g. biguanide and thiazolidinedione (O'Toole et al. 2012). Unfortunately, they are contraindicated in patients with ESRD. Recent research has reported that the metabolic effect of an Angiotensin II receptor blocker (ARB), Telmisartan, has a unique pharmacological characteristic by its affinity for Angiotensin II Receptor-1 (ATR-1), but not for other receptors (adenosine, adrenergic, dopaminergic, endothelin, histamine, muscarinic, neurokinin, neuropeptide Y, or serotoninergic). Telmisartan is a partial selective agonist on PPARγ, which regulates lipid and carbohydrate metabolism. There are studies showing the ability of Telmisartan on improving insulin resistance by decreasing plasma insulin and HOMA IR (Kurtz & Pravenec 2004). Other parameters to indicate the existence of insulin resistance are lipid profile and proinflammatory cytokines level. This research aimed to examine the effect of Telmisartan on lipid profiles and inflammatory marker in patients with ESRD and hypertension.

2 MATERIAL AND METHOD

2.1 *Study design*

It was an observational research with a cohort prospective method aimed to investigate the Telmisartan effects on lipid profiles (cholesterol, LDL, HDL and TG), and inflammatory marker (CRP) on hemodialysis patients with hypertension.

2.2 *Subject*

Subject of present study were patients with ESRD and hypertension (HT) undergoing regular hemodialysis (HD) and fulfilling the inclusion criteria

including: (1) is undergoing regular HD with minimum twice a week during the last three months; (2) has pre-dialysis blood pressure >140/90: (3) the first time of consuming Telmisartan; (4) is willing to join the research and has signed the informed consent. The subjects' exclusion criterion was the subject who has fasting blood glucose >130 mg/dL. Dropout criteria were as follows: non-compliance, allergic, and/or suffering from medicine side effects; subjects were no longer going to undergo hemodialysis; patient died during the research. The number of samples in the present study was 15–20 subjects (pilot research).

2.3 *Sampling technique*

Sampling technique in this research was using non-probability-sampling with consecutive sampling method.

2.4 *Statistical analysis*

The data were statistically analyzed by paired t-test and/or Wilcoxon test.

3 RESULT AND DISCUSSION

There were 16 subjects (12 men and four women) recruited in HD Unit Bhayangkara Hospital Surabaya. The average of the subject age and Body Mass Index (BMI) were 45 years old and 22.85, respectively. The distribution of sexes, ages and BMI are shown in Table 1.

The lipid profiles examined in the present study were cholesterol, HDL, LDL and triglycerides. In the beginning of the study, it was found that the mean levels of cholesterol, TG, HDL and LDL were in normal range, which were 154.88 mg/dl, 82.44 mg/dl, 42.69 mg/dl, and 90.44 mg/dl, respectively (Table 2). However, there were two patients with cholesterol, TG and LDL above normal limit. After three months of treatment with Telmisartan, the mean levels of cholesterol, TG, HDL and LDL were 127.31 mg/dl, 74 mg/dl, 50.06 mg/dl and 74.56 mg/dl, respectively. Since the distribution of the data was normal, paired t test was conducted to determine the statistical difference in the level of cholesterol, HDL and LDL. The present study showed that Telmisartan therapy for three months significantly decreased cholesterol, HDL and LDL in patients with ESRD and hypertension ($p < 0.001$). On the other hand, since the data distribution of triglycerides was not normal, we conducted Wilcoxon test. P value was 0.043 ($p < \alpha$, $\alpha = 0.05$) indicating Telmisartan therapy for three months did not significantly decrease triglyceride level.

Table 1. The demographic data of the subjects.

Characteristics		Result	
		Number	Percentage (%)
Sex	Men	12	75
	Women	4	25
Age	20–40	6	37.5
	40–60	10	62.5
BMI	18.5–25	13	81.25
	25–30	3	18.75

Table 2. Lipid profile at pre- and post-therapy of Telmisartan.

Sample		Median ± SD Range	p value
Cholesterol	Pre	154.88 ± 33.86 mg/dl 244–85 mg/dl	p = 0.001
	Post	127.31 ± 21.85 mg/dl 182–84	
TG	Pre	82.44 ± 39.49 mg/dl 230–27 mg/dl	p = 0.187
	Post	74.00 ± 34.38 mg/dl 192–20 mg/dl	
HDL	Pre	42.69 ± 9.23 mg/dl 73–24 mg/dl	p = 0.011
	Post	50.06 ± 7.06 mg/dl 70–36 mg/dl	
LDL	Pre	90.44 ± 24.12 mg/dl 172–52	p = 0.010
	Post	74.56 ± 15.13 118–44	

The mean level of CRP before Telmisartan therapy was normal (0.47 mg/dl; Fig. 1). After a 3-month Telmisartan therapy, the mean level of CRP decreased to 0.34 mg/dl. However, there are six subjects (37.5%) with an increase CRP level. Wilcoxon test showed that there was no statistical difference between CRP level in pre- and post-therapy with Telmisartan ($p = 0.437$; Figure 1).

Telmisartan activities on insulin resistance, lipid profiles, and inflammation are based on its ability as agonis parsial PPARɣ. PPARɣ is one of the receptors for nuclear hormone that play an important role as transcription factor in the regulation of carbohydrate metabolism, lipid metabolism, and inflammation. PPARɣ is commonly expressed in adipocyte tissue and smaller expression in vascular smooth muscle cells, endothelium, and monocytes (Kurtz & Pravenec 2004). The activity of Telmisartan is closely related to the molecular structure

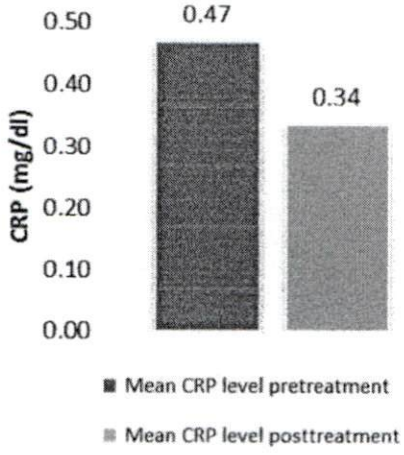

Figure 1. CRP profile at pre- and post-therapy with Telmisartan.

resembling pioglitazone, one of thiazolidinedione. Telmisartan exhibits 25–30% of pioglitazone ability to activate PPARɣ (Kurtz & Pravenec 2004).

The activation of PPARɣ increases the expression of many kinds of genes as well as enzymes related to carbohydrate metabolism (adiponectine, glucokinase, GLUT-4 glucose transporter) and lipid metabolism (lipoprotein lipase, adipocyte fatty acid transporter protein, fatty acyl CoA synthase, malic enzyme). Likewise, the activation of PPARɣ suppresses the activity of inflammatory factor TNF-α, which suppresses insulin sensitivity through insulin signal transduction disorders (Bouskila et al. 2005).

The decrease in insulin resistance shown by the notable changes in most of the lipid profiles (LDL, HDL, cholesterol) after 3-months therapy with Telmisartan demonstrates the theoretical hypothesis on the activity of Telmisartan on PPARɣ. This activity on PPARɣ showed that Telmisartan potentially affects the regulation of carbohydrate metabolism, lipid metabolism and inflammation (Kurtz & Pravenec 2004). However, the present study failed to show a suppressing effect of Telmisartan on CRP level.

CRP is one of the main inflammatory markers related to cardiovascular mortality and infection on patients with HD (Kawaguchi et al. 2011). The increase of CRP level in ESRD subjects is particularly caused by chronic inflammation and oxidative stress. However, low albumin serum, calcium level, high BMI and uric acid may also play important roles in increasing CRP level (Kawaguchi et al. 2011). Thus, the inadequate effect of Telmisartan on improving CRP level in the present study might be caused by other factors that were not well controlled before the study.

4 CONCLUSION

From the present study, it can be concluded that Telmisartan has a promising prospect to be used for decreasing lipid profiles in patients with ESRD. Further study is needed to strengthen the present findings.

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