



MINISTRY OF HEALTH MALAYSIA
PHARMACEUTICAL SERVICES PROGRAMME

PHARMACY RESEARCH REPORTS

Volume 4 • Issue 2 • November 2021

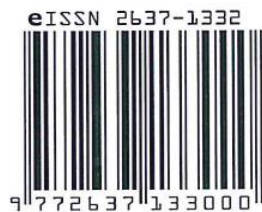
PHARMACY RESEARCH REPORTS

Volume 4 • Issue 2 • November 2021

The Pharmacy Research Reports is a peer-reviewed journal published by the Pharmaceutical Services Programme, Ministry of Health Malaysia (MOH). This is an International Standard Serial Number (ISSN) registered publication with the National Bibliography Centre, National Library of Malaysia. This document contains compilation of peer-reviewed original scientific research articles of pharmacy related research conducted in the MOH or by MOH pharmacists and other professionals. All research included in this report were registered with the National Medical Research Register (NMRR) and ethics approvals had been obtained from the Medical Research and Ethics Committee (MREC). The opinions expressed in all articles are the authors' own and do not necessarily reflect the view of the Pharmaceutical Services Programme, Ministry of Health Malaysia.

November 2021

© Pharmaceutical Services Programme, Ministry of Health Malaysia



No. Siri Penerbitan KKM
MOH/S/FAR/52.21(TR)-e

No. Pendaftaran Dokumen Program Perkhidmatan Farmasi
D-RR-97

Editorial Address:

Editor in Chief

Pharmacy Research Reports

Pharmacy Policy and Strategic Planning Division

Pharmaceutical Services Programme

Ministry of Health Malaysia

Lot 36, Jalan Universiti, 46200 Petaling Jaya, Selangor, Malaysia

Tel : (603) 7841 3200

Fax : (603) 7968 2222

Email : rndfarmasi@moh.gov.my

Website : <https://www.pharmacy.gov.my> / <https://research.pharmacy.gov.my>

PHARMACY RESEARCH REPORTS

Volume 4 • Issue 2 • November 2021

EDITORIAL BOARD

Advisor

Mdm. Siti Aisah Bahari
&
MOH Pharmacy Research and Development (R&D) Committee

Editor in Chief

Dr. Abdul Haniff Mohd Yahaya

Reviews Editor

Ho See Wan

Dr. Nor Ilham Ainaa Muhsin

Secretariat

Ho See Wan

Dr. Nor Ilham Ainaa Muhsin

MOH PHARMACY RESEARCH AND DEVELOPMENT (R&D) COMMITTEE 2021-2023

Chairperson

Mdm. Siti Aisah Bahari
Director of Pharmacy Policy and Strategic Planning Division

Secretary

Dr. Abdul Haniff Mohd Yahaya
Deputy Director, Pharmacy Policy and Strategic Planning Division

Committee Members

Mr. Manzatul Azrul Azrie Sulaiman
Pharmacy Enforcement Division

Dr. Jazlina Liza Dato Jamaludin
National Pharmaceutical Regulatory Agency

Mdm. Datcayani Ramadoo
Pharmacy Board Malaysia

Mdm. Norazila Abd. Ghani
Hospital Jitra, Kedah

Mdm. Hazlinda Abu Hassan
Melaka State Health Department

Mdm. Mastura Ahmad
Hospital Tengku Ampuan Afzan, Pahang

Mr. Gobi Hariyanayagam Gunasekaran
Hospital Seri Manjung, Perak

Mdm. Asmahani Ramelan
Hospital Tengku Ampuan Rahimah Klang, Selangor

Mr. Jerry Liew Ee Siung
Hospital Queen Elizabeth, Sabah

Mdm. Soo Bee Kuan
WP Labuan Health Department

Dr. Rahela Ambaras Khan
Hospital Kuala Lumpur

Dr. Nur Liyana Zainal Bahrin
Pharmacy Practice and Development Division

Ms. Nur Ain A Rashid
Pharmacy Policy and Strategic Planning Division

Mdm. Zahrina Abdul Kadir
Johor State Health Department

Mdm. Nazmi Liana Azmi
Hospital Raja Perempuan Zainab II, Kelantan

Mdm. Nurrul Salwa Saleh
Hospital Tuanku Ampuan Najihah, Negeri Sembilan

Mr. Teoh Chee Jia
Hospital Seberang Jaya, Penang

Mdm. Hazlin Syafinar Hussein
Perlis State Health Department

Ms. Mazlina Mukhtar
Hospital Sultanah Nur Zahirah, Terengganu

Dr. Samuel Ting Chuo Yew
Sarawak State Health Department

Dr. Navin Kumar Loganadan
Hospital Putrajaya, WP Kuala Lumpur & Putrajaya

Mr. Muhammad Fakhurazi Ahmad Fadzi
National Cancer Institute

Secretariat

Mdm. Chan Pui Lim
Pharmacy Policy and Strategic Planning Division

Ms. Ho See Wan
Pharmacy Policy and Strategic Planning Division

Dr. Nor Ilham Ainaa Muhsin
Pharmacy Policy and Strategic Planning Division

Dr. Noraini Nordin
Pharmacy Policy and Strategic Planning Division

Ms. Mary Chok Chiew Fong
Pharmacy Policy and Strategic Planning Division

Mr. Tineshwaran Velvanathan
Pharmacy Policy and Strategic Planning Division

Mdm. Azzy Iyzati Ahmad Shanizza
Pharmacy Policy and Strategic Planning Division

Mdm. Siti Nur Su'aidah Nasarudin
Pharmacy Policy and Strategic Planning Division

PHARMACY RESEARCH REPORTS

Volume 4 • Issue 2 • November 2021

ACKNOWLEDGEMENT

The Editorial Board of the Pharmacy Research Reports wishes to express our deepest appreciation to the reviewers for their valuable time and efforts in reviewing the manuscripts.

List of Reviewers:

Mdm. Azzy Iyzati Ahmad Shanizza

Mdm. Chan Pui Lim

Mr. Gobi Hariyanayagam a/l Gunasekaran

Ms. Ho See Wan

Dr. Navin Kumar Loganadan

Ms. Mary Chok Chiew Fong

Mdm. Nazmi Liana Azmi

Dr. Nor Ilham Ainaa Muhsin

Dr. Samuel Ting Chuo Yew

PHARMACY RESEARCH REPORTS

Volume 4 • Issue 2 • November 2021

CONTENTS

	<i>page</i>
1. A Cross-Sectional Survey of Attitude, Perception and Interest in Conducting Pharmacy Practice Research among the Northern States Enforcement Pharmacists in Malaysia	1
<i>Vinoedh Naidu Raja Gopal, Lee Boon Sin, A. Thanalekshumi Appadorai, Dali Ismail, Rohaya Mahmud, Mokhtar Abdullah</i>	
2. The Prevalence of Supratherapeutic International Normalised Ratio (INR) in Warfarin Use and Its Associated Factors among Atrial Fibrillation Patients in Hospital Teluk Intan, Perak	9
<i>Loo Sook Peng, Fatimatuzzahra' Abd Aziz, Nur Aizati Athirah Daud</i>	
3. Depression, Anxiety and Stress (DAS), and Workplace Spirituality among Pharmacists and Pharmacist Assistants in the state of Perlis, Malaysia	19
<i>Soo Pei Pei, Mohd Shainol Azmar Kassim, Nur Ainin Aqilah Mohd Rafi, Nursyuhaidah Ramli, Raja Masturah Raja Sulaiman, Dandaithapani Thyagarajan</i>	
4. Perceptions of Type 2 Diabetes Mellitus Patients towards Insulin Therapy and Willingness to Accept Insulin Therapy at the Public Health Clinics in South Seberang Perai District, Malaysia	29
<i>Balamurugan Supparamaniam, Norul Adlin Abu Safran, Nor Hidayah Ruzalle, Loh Yi Song, Asiah Idris, Lee Li San, Teoh Hui Pin, Teng Jie Ying</i>	
5. Medication Errors Understanding among the Healthcare Providers at the Health Clinics in Labuan Federal Territory	38
<i>Mohd Arrif Md Zahary, Eddie Ha Hsiao Lung, Farah Ayuni Ghazali, Caroline Esther Paul</i>	

A Cross-Sectional Survey of Attitude, Perception and Interest in Conducting Pharmacy Practice Research among the Northern States Enforcement Pharmacists in Malaysia

Vinoedh Naidu Raja Gopal¹, Lee Boon Sin¹, A. Thanalekshumi Appadorai¹, Dali Ismail¹, Rohaya Mahmud¹, Mokhtar Abdullah¹

¹ Kedah Pharmacy Enforcement Branch, Kedah State Health Department, Ministry of Health Malaysia

Abstract

Introduction: Pharmacy practice research becomes an essential element in Malaysian pharmacy practice. An increasing number of pharmacy practice research findings proved its importance in policy decision making and improving health services.

Objectives: This study aimed to determine the attitude, perception and interest among the enforcement pharmacists in conducting research and to compare with their demographic factors.

Methods: A cross-sectional survey was conducted using a validated self-administered questionnaire that assess the attitude, perception and interest to conduct pharmacy practice research among the enforcement pharmacists in four northern states in Malaysia namely Kedah, Perlis, Penang and Perak. Descriptive analysis was used to analyse the attitude, perception and interest responses. Independent samples t-test and one-way ANOVA and were used to compare the attitude, perception and interest based on demographic factors.

Results: A total of 120 enforcement pharmacists responded to the questionnaire (response rate: 94.5%). The attitudes, perception and interest were moderate. The mean scores [\pm standard deviation (SD)] of attitudes, perception and interest were 3.05 ± 0.56 , 3.26 ± 0.51 and 2.94 ± 0.77 respectively. The main barrier to research was not having enough time to conduct research (73.3%) and the least reported barrier was other reason – forced to do (0.8%). There was no significant association between the age, gender and working experience with the attitude, perception and interest. No significant association was also observed in the perception and interest among the enforcement pharmacists with their prior research experience. However, there was a statistically significant association between the attitude and prior research experience ($p=0.045$).

Conclusion: The enforcement pharmacists in Northern Malaysia had moderate attitude, perception and interest in conducting pharmacy practice research and those with prior research experience had more positive attitude to conduct research.

Keywords: attitude, perception, interest, enforcement pharmacists, pharmacy practice, Malaysia

NMRR ID: NMRR-20-677-53214

Corresponding Author: Vinoedh Naidu Raja Gopal

Kedah Pharmacy Enforcement Branch, Kedah State Health Department, Jalan Kuala Kedah, 05400 Alor Setar, Kedah.

Email: vinoedh@moh.gov.my

Introduction

Research is an important aspect of pharmaceutical services and health care delivery by providing innovative ideas, valuable information, transformation and evidence to support policy decision making and improve health services. Pharmacy practice in Malaysia compromises pharmaceutical care to patients at the primary and secondary care levels as well as enforcement of relevant acts and regulations pertaining to pharmaceutical products and cosmetics. There is a strong commitment by the Pharmacy Services Programme of Ministry of Health Malaysia (MOH) to encourage all pharmacists to conduct research in addition to their routine job, in line with the changing demands of the population and the advancement of digital technology. Globally, health systems face challenges in terms of access to needed medicines,

optimising medicines use and reducing unwanted risk. Thus, useful research outcomes will improve population health and economic well-being besides facilitating health policies.

The increasing trend of conducting research among the pharmacists are seen lately. There were only about 50% pharmacy facilities within MOH conducting research in year 2015, but this had increased to 95% in 2020 (1). Meanwhile, the first Pharmacy Research Reports was published in 2018 by the Pharmaceutical Services Programme, marking a milestone to collect and publish the research findings by the pharmacists in MOH, which also proved the significance of pharmacy practice research in Malaysia (2). This encourages and intensifies knowledge sharing via publishing research findings.

A large number of small-scaled research are being conducted at the hospitals and health facilities by a mixture of trained and inexperienced pharmacy researchers (3), who sometimes repeat similar researches in different facilities. However, overcoming this is not easy because pharmacists must have adequate research skills and understanding of research gaps. Furthermore, there are limited researches in the field of pharmacy enforcement to serve as references to improve pharmacy enforcement practices. Good researches are important to address critical concerns.

Several studies from the other countries showed that although the pharmacists were aware of research, they were less likely to get involved in research activities (4,5). This situation is expected to be worse among the enforcement pharmacists as their job scopes are different from other pharmacists. The enforcement pharmacists are mainly involved in enforcement and prevention activities, control of licensing, monitoring activities, and consumer awareness activities to reduce the demand for unsafe or hazardous products (6). So far, no studies have addressed the need of pharmacy research among the pharmacy enforcement officers worldwide. This study's aim was to assess the attitude, perception and interest of enforcement pharmacists in conducting pharmacy practice researches. The results of this research will be useful for the enforcement pharmacists and policy makers to improve their involvement in pharmacy research.

Methods

This cross-sectional study was carried out from August to October 2020 in four northern states in Malaysia namely Kedah, Perlis, Penang and Perak. The questionnaire for this study was adapted from similar studies that was done in Saudi Arabia and Ethiopia (4,7). The permissions from the authors were obtained to use and modify the questionnaires as the original questionnaires were conducted in different settings in Saudi Arabia and Ethiopia. This newly developed questionnaire was validated through content validation by three subject matter experts (SME). A pilot study was conducted among 20 selected enforcement pharmacists from Kedah. The internal consistency by Cronbach's alpha of attitude, perception and interest in conducting research were 0.775, 0.758 and 0.954 respectively in this study. Therefore, all Cronbach's alpha scores were acceptable for modified instruments. The pilot study results were also included in the final analysis.

This questionnaire consists of five sections where section A collected the demographic factors such as age, gender, academic qualification, working experience in years and prior research experience. Section B, C and D contained ten questions each to collected responses on the attitude, perception and interest in conducting pharmacy practice research using 5-point Likert's scale. Scores were assigned to the answers, in which 1=strongly disagree, 2=disagree, 3=neutral, 4=agree and 5=strongly agree. There were some negative statements and these were reversely coded before the analysis. The mean (\pm standard deviation (SD)) scores were calculated, with the highest possible mean score being 5.00 and lowest possible mean score was 1.00. The scores were classified into low, moderate and high by dividing the difference between the highest and lowest possible mean score by 3 to give an interval of 1.33. Mean score of 1.00-2.33, 2.34-3.67 and 3.68-5.00 was interpreted as low, moderate and high level of attitude, perception and interest in conducting research (8). In section E, the barriers to conducting research was investigated.

This study was approved by the MOH Medical Research and Ethics Committee (MREC) with the National Medical Research Registry (NMRR) registration number of NMRR-20-677-53214. All 127 practising enforcement pharmacists from the selected Malaysian northern states were included. The questionnaires were sent out by registered mail to the respective offices and follow-up with the states' representatives was done every week.

Data was analysed using Statistical Package for Social Science (SPSS) version 23.0. Descriptive analysis focused on frequencies and percentages while independent samples t-tests and one-way analysis of variance (ANOVA) were utilised to determine the differences between the selected demographic variables. The statistical significance level was set at $p < 0.05$. Academic qualification was not analysed and discussed as 90% of the respondents were having bachelor academic qualification.

Results

A total of 120 responses were received (response rate 94.5%) and analysed. The demographic characteristics of the study population were reported in Table 1. Majority of the respondents were between 31-35 years old (47.5%), male (53.3%), have bachelor academic qualification (90%), working experience of 4-6 years (28.3%) and with prior research experience (65.8%).

Most of the responses to the attitude, perception and interest to conduct pharmacy practice research were in the moderate level, with only seven out of 30 attitude, perception and interest statements were positively or negatively responded (levels: low = 1.00–2.33, moderate = 2.34–3.66, high = 3.67–5.00).

The attitude of the respondents to conduct pharmacy practice research was moderate with the mean score of 3.05 (SD 0.558, range 2.56–3.64). The statement with the highest mean score was '*Research is of little importance in Malaysia*' and this was a negative statement. The lowest mean score statement was '*I am confident to conduct research*'.

The perception of the respondents to conduct pharmacy practice research was moderate with the mean score of 3.26 (SD 0.507, range 2.45–4.13). The highest mean score statement was '*Research is important to improve health service delivery*'. The lowest mean score statement was '*My daily activities prevent me from doing research*' and this was a negative statement.

The interest of the respondents to conduct pharmacy practice research was also moderate with the mean score of 2.94 (Std.Deviation = 0.769, range 2.78 – 3.12). The highest mean score statement was '*Generating research ideas*'. The lowest mean score statement was '*Giving an oral presentation*'.

When examining the barriers in conducting research, it was found that the main barrier reported was no enough time (73.3%), followed by no personal interest and lack of knowledge (62.5%) (Table 5). In terms of association between the characteristics of the enforcement pharmacist with the attitude to conduct pharmacy practice research, it was found that there was a significant association between prior research experience ($p=0.045$) and attitude. There was no significant association between the demographic characteristics of the enforcement pharmacist with their perception and interest to conduct pharmacy practice research (Table 6).

Table 1: Respondents' demographic characteristics (n=120)

Demographic variables	n	(%)
Age group		
25 - 30 years	33	(27.5)
31 - 35 years	57	(47.5)
36 years and above	30	(25.0)
Gender		
Male	64	(53.3)
Female	56	(46.7)
Current academic qualification		
Bachelor	108	(90.0)
Master	12	(10.0)
Experience as enforcement pharmacist		
1 - 3 years	31	(25.8)
4 - 6 years	34	(28.3)
7 - 9 years	28	(23.3)
10 years and above	27	(22.5)
Prior research experience		
Yes	79	(65.8)
No	41	(34.2)

Table 2: Attitude towards pharmacy practice research (n=120)

No.	Statement	n (%)					Mean	SD
		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree		
B1	Being involved in research is important to my career	2 (1.7)	12 (10.0)	56 (46.7)	43 (35.8)	7 (5.8)	3.34	0.804
*B2	Research is of little importance to me	5 (4.2)	29 (24.2)	60 (50.0)	20 (16.7)	6 (5.0)	3.06	0.882
B3	I feel that it is my professional duty to be involved in research	3 (2.5)	17 (14.2)	58 (48.3)	33 (27.5)	9 (7.5)	3.23	0.877
*B4	Research is of little relevance to enforcement pharmacists'	9 (7.5)	34 (28.3)	51 (42.5)	23 (19.2)	3 (2.5)	3.19	0.919
*B5	Research is of little importance in Malaysia	26 (21.7)	49 (40.8)	23 (19.2)	20 (16.7)	2 (1.7)	3.64	1.052
*B6	Research is more suited to academics rather than enforcement pharmacists'	6 (5.0)	26 (21.7)	32 (26.7)	34 (28.3)	22 (18.3)	2.67	1.155
B7	I already underwent research training courses	9 (7.5)	20 (16.7)	46 (38.3)	39 (32.5)	6 (5.0)	3.11	0.994
B8	Involving in research is a part of my practice	6 (5.0)	26 (21.7)	62 (51.7)	20 (16.7)	6 (5.0)	2.95	0.887
*B9	I don't have time to think about research	7 (5.8)	20 (16.7)	45 (37.5)	30 (25.0)	18 (15.0)	2.73	1.090
B10	I am confident to conduct research	14 (11.7)	47 (39.2)	43 (35.8)	10 (8.3)	6 (5.0)	2.56	0.977
Overall							3.05	0.558

Abbreviation: SD – standard deviation.

* Negative statements.

Table 3: Perception towards pharmacy practice research (n=120)

No.	Statement	n (%)					Mean	SD
		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree		
C1	Research should be a high priority for pharmacist	3 (2.5)	19 (15.8)	48 (40.0)	44 (36.7)	6 (5.0)	3.26	0.874
C2	It is important to be kept informed of the research relevant to the practice of pharmacy	1 (0.8)	2 (1.7)	37 (30.8)	62 (51.7)	18 (15.0)	3.78	0.747
C3	My daily practice is influenced by evidence based pharmacy practice research	10 (8.3)	24 (20.0)	49 (40.8)	29 (24.2)	8 (6.7)	3.01	1.025
*C4	Pharmacy research findings are irrelevant to me as an enforcement pharmacist	7 (5.8)	46 (38.3)	44 (36.7)	14 (11.7)	9 (7.5)	3.23	0.994
C5	Research is important to improve health service delivery	1 (0.8)	0 (0.0)	17 (14.2)	66 (55.0)	36 (30.0)	4.13	0.709
C6	Research is important for my recognition	7 (5.8)	12 (10.0)	67 (55.8)	26 (21.7)	8 (6.7)	3.13	0.898
C7	Research is important for my self-satisfaction	13 (10.8)	21 (17.5)	57 (47.5)	27 (22.5)	2 (1.7)	2.87	0.943
*C8	My daily activities prevent me from doing research	3 (2.5)	14 (11.7)	40 (33.3)	40 (33.3)	23 (19.2)	2.45	1.011
C9	I would require supervision to do research	1 (0.8)	3 (2.5)	26 (21.7)	66 (55.0)	24 (20.0)	3.91	0.767
C10	I am prepared to make time to do research during working hours	13 (10.8)	26 (21.7)	49 (40.8)	28 (23.3)	4 (3.3)	2.87	1.004
Overall							3.26	0.507

Abbreviation: SD – standard deviation.

* Negative statements.

Table 4: Interest to conduct pharmacy practice research (n=120)

No.	Statement	n (%)					Mean	SD
		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree		
D1	Generating research ideas	4 (3.3)	22 (18.3)	57 (47.5)	30 (25.0)	7 (5.8)	3.12	0.891
D2	Finding relevant literature	8 (6.7)	24 (20.0)	57 (47.5)	28 (23.3)	3 (2.5)	2.95	0.897
D3	Writing a research proposal	9 (7.5)	26 (21.7)	62 (51.7)	20 (16.7)	3 (2.5)	2.85	0.876
D4	Using quantitative research methods (e.g. RCTs, cohort studies, surveys, questionnaires)	10 (8.3)	19 (15.8)	59 (49.2)	27 (22.5)	5 (4.2)	2.98	0.944
D5	Using qualitative research methods (e.g. focus groups, interviews)	11 (9.2)	20 (16.7)	60 (50.0)	26 (21.7)	3 (2.5)	2.92	0.922
D6	Analysing results	8 (6.7)	19 (15.8)	59 (49.2)	31 (25.8)	3 (2.5)	3.02	0.889
D7	Interpreting results	8 (6.7)	15 (12.5)	59 (49.2)	35 (29.2)	3 (2.5)	3.08	0.885
D8	Giving an oral presentation (e.g. national or international conference)	14 (11.7)	30 (25.0)	49 (40.8)	22 (18.3)	5 (4.2)	2.78	1.014
D9	Writing final research thesis	11 (9.2)	28 (23.3)	57 (47.5)	20 (16.7)	4 (3.3)	2.82	0.935
D10	Publishing research in academic journals	9 (7.5)	26 (21.7)	59 (49.2)	24 (20.0)	2 (1.7)	2.87	0.879
Overall							2.94	0.769

Abbreviation: SD – standard deviation.

Table 5: Barriers in conducting pharmacy practice research (n=120)

	n (%)
No personal interest	75 (62.5)
Not enough staff	38 (31.7)
Not aware of opportunity	17 (14.2)
Not enough time	88 (73.3)
Never been asked to	3 (2.5)
Lack of incentives	41 (34.2)
Lack of knowledge	75 (62.5)
Lack of support	47 (39.2)
Lack of research facilities	41 (34.2)
Others	1 (0.8)

Note: Respondents were allowed to choose more than one response.

Table 6: Association between demographic characteristics and attitude, perception and interest scores (n=120)

Demographic variables	n (%)	Attitude score, mean (SD)	t / F statistics	p-value	Perception score, mean (SD)	t / F statistics	p-value	Interest score, mean (SD)	t / F statistics	p-value
Age group ¶										
25 - 30 years	33 (27.5)	3.082 (0.517)	0.129	0.88	3.342 (0.462)	0.606	0.547	2.982 (0.718)	0.08	0.923
31 - 35 years	57 (47.5)	3.049 (0.576)			3.249 (0.539)			2.93 (0.846)		
36 years and above	30 (25.0)	3.01 (0.581)			3.01 (0.581)			2.907 (0.686)		
Gender §										
Male	64 (53.3)	3.083 (0.581)	0.723	0.471	3.298(0.494)	0.79	0.431	3.047 (0.675)	1.665	0.099
Female	56 (46.7)	3.009 (0.532)			3.225 (0.524)			2.814 (0.854)		
Experience as enforcement pharmacist ¶										
1 - 3 years	31 (25.8)	3.126 (0.461)	0.291	0.832	3.429 (0.449)	1.61	0.189	2.887 (0.662)	0.566	0.638
4 - 6 years	34 (28.3)	3.003 (0.595)			3.118 (0.573)			2.988 (0.913)		
7 - 9 years	28 (23.3)	3.021 (0.595)			3.182 (0.406)			2.814 (0.688)		
10 years and above	27 (22.5)	3.044 (0.592)			3.256 (0.557)			3.063 (0.783)		
Prior research experience §										
Yes	79 (65.8)	3.115 (0.602)	2.029	0.045	3.272 (0.519)	0.238	0.812	2.973 (0.848)	0.773	0.441
No	41 (34.2)	2.916 (0.44)			3.249 (0.49)			2.871 (0.592)		

Abbreviation: SD – standard deviation.

¶ One-way Anova; § Independent T test.

Discussion

Research among the enforcement pharmacists are relatively limited. To date, there has been limited published data on the attitude, perception and interest of the enforcement pharmacists to conduct pharmacy practice research. It was therefore a timely study to improve the involvement of enforcement pharmacists in pharmacy researches.

In this study, majority of the enforcement pharmacists expressed a moderate attitude, perception and interest towards pharmacy practice research. There was no significant association between the demographic factors of enforcement pharmacist with attitude, perception and interest to do research among enforcement pharmacist. This clearly showed that most of the enforcement pharmacists were indifferent towards pharmacy practice research. This can be debatable as enforcement pharmacists' attitude, perception and interest towards pharmacy practice research might be different from others like hospital pharmacists, clinical pharmacists or community pharmacists even though they had the same background of education. Another underlying reason would be the different job scopes of enforcement pharmacists.

However, those with prior experience in research had more positive attitudes towards research. The percentage of enforcement pharmacists with prior research experience in this study was higher (65.8%) compared to the population in other studies where the rate ranged from 9% to 50% (9,10). This reflected that involvement in research activities was not a new thing among the pharmacy enforcement officers consequential to research activities done during their undergraduate years in the pharmacy school.

In terms of the attitude and perception, the respondents generally felt that research is important but they were less confident to do it. The daily activities of enforcement officers may not provide a conducive environment to conduct research. This was evident that majority of the respondent reported time as a barrier to conduct research. Most of the respondents were also interested in generating research ideas but had reservation about presenting the research orally.

Enforcement pharmacists who participated in this survey appeared to understand the importance, relevance and value of pharmacy practice research. However, since they were not directly involved with patient care and health services delivery, their attitude, perception and interest towards pharmacy practice research may be moderate. Nevertheless, the barriers related to time, knowledge, support, incentives, facilities and opportunities identified in this study were quite similar to other studies (9). When a research was conducted as a compulsory requirement or request by the management, this may limit the contribution (5).

This research is the first study of Malaysian enforcement pharmacists' attitude, perception and interest to research with excellent response rate of (94.5%). There were some in this study. Firstly, this study is only done in northern region and could not be generalised nationally as different region may have different response. Besides that, the the respondent of this survey was mainly between 31 to 35 years old who are upper young adult compared the general enforcement workforce whom age could range between 22 to 60 years old. Thus, the result of this study might not generalize the enforcement pharmacist population in Malaysia.

Conclusion

Most of the enforcement pharmacists in the northern region of Malaysia had moderate attitude, perception and interest towards pharmacy practice research. Our result indicated that only those with prior research experience had better attitude towards research. The top three main barriers for enforcement pharmacists to conduct pharmacy practice research were no enough time, no personal interest and lack of knowledge. Therefore, there is need for the MOH and senior pharmacists to encourage pharmacists to conduct pharmacy practice research by addressing the barriers.

Acknowledgement

We would like to thank the Director General of Health Malaysia for his permission to publish this article. We would also like to acknowledge the kindness of Akshaya Srikanth Bhagavathula and Khizra Sultana for providing and allowing us to use their questionnaire instruments. Lastly, we would like to thank the State Health Directors of Kedah, Perlis, Penang and Perak, our colleagues and respondents for supporting this study.

Conflict of Interest Statement

The study was undertaken within the MOH and is not funded by any organisation. The authors declared no conflict of interest.

References

1. Pharmaceutical Services Programme. Pharmacy Programme Strategic Plan 2017-2020 [online]; 2017 [cited Jan 28 2020]. Available from: <https://www.pharmacy.gov.my/v2/sites/default/files/document-upload/2017-2020-web.pdf>
2. Pharmaceutical Services Programme. Pharmacy Research Reports [online]; 2018 [cited Nov 28 2020]. Available from: <https://www.pharmacy.gov.my/v2/sites/default/files/document-upload/moh-pharmacy-researchreports-vol1-2018.pdf>.
3. Pharmaceutical Services Programme. Pharmacy Research Priorities in Malaysia [online]; 2018 [cited Jan 28 2020]. Available from: https://www.pharmacy.gov.my/v2/sites/default/files/document-upload/pharmacy-research-priorities-malaysia-2018_0.pdf.
4. Sultana Khizra, Al Jeraisy Majed, Al Ammari Maha, Patel Rahul, Zaidi Syed Tabish R. Attitude, barriers and facilitators to practice-based research: cross-sectional survey of hospital pharmacists in Saudi Arabia. *J Pharm Policy Pract.* 2016;9(4):4. doi: 10.1186/s40545-016-0052-z, PMID 26877877.
5. Peterson GM, Jackson SL, Fitzmaurice KD, Gee PR. Attitudes of Australian pharmacists towards practice-based research. *J Clin Pharm Ther.* 2009;34(4):397-405. doi: 10.1111/j.1365-2710.2008.01020.x. PMID 19583672.
6. Pharmaceutical Services Programme 2020. Pharmacy Enforcement Division [online] [cited Dec 16 2020]. Available from: <https://www.pharmacy.gov.my/v2/en/content/pharmacy-enforcement-division.html>.
7. Bhagavathula AS, Gebreyohannes EA, Gebresillassie BM, Erku DA, Negesse CT, Belay YB. Community pharmacists' interest in and attitude to pharmacy practice research in Ethiopia: A cross-sectional study. *PLOS ONE.* 2017;12(6):e0178919. doi: 10.1371/journal.pone.0178919. PMID 28617834.
8. Polit D, et al. *Nursing research: principle and method.* 6th ed. Philadelphia: Lippincott Company, P.P; 1999. p. 416-417.
9. Elkasseem W, Pallivalapila A, Al Hail M, McHattie L, Diack L, Stewart D. Advancing the pharmacy practice research agenda: views and experiences of pharmacists in Qatar. *Int J Clin Pharm.* 2013;35(5);Suppl 5:692-6. doi: 10.1007/s11096-013-9802-z. PMID 23743706.
10. Awaisu A, Alsalmiy N. Pharmacist's involvement and attitudes towards pharmacy practice research: A systematic review of the literature. *Res Soc Admin Pharm.* 2015;11(6);Suppl 6:725-48. doi: 10.1016/j.sapharm.2014.12.008.
11. Rosenbloom K, Taylor K, Harding G. Community pharmacists' attitudes towards research. *Int J Pharm Pract.* 2011;8(2):103-10. doi: 10.1111/j.2042-7174.2000.tb00994.x.
12. Armour C, Brilliant M, Krass I. Pharmacists' views on involvement in pharmacy practice research: Strategies for facilitating participation. *Pharm Pract.* 2007;5(2):59-66. doi: 10.4321/s1886-36552007000200002, PMID 25214919.
13. Roberts R, et al. Pharmacy research has an impact on each and every pharmacist. *The Pharmaceutical Journal.* 2010;284:267-8.
14. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? *Indian J Psychol Med.* 2013;35(2):121-6. doi: 10.4103/0253-7176.116232, PMID 24049221.

The Prevalence of Supratherapeutic International Normalised Ratio (INR) in Warfarin Use and Its Associated Factors among Atrial Fibrillation Patients in Hospital Teluk Intan, Perak

Loo Sook Peng¹, Fatimatu Zahra' Abd Aziz², Nur Aizati Athirah Daud²

¹ Hospital Teluk Intan, Perak, Ministry of Health Malaysia

² Universiti Sains Malaysia, Pulau Pinang

Abstract

Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice. Data on the prevalence of supratherapeutic International Normalised Ratio (INR) following warfarin use among AF patients is only available for countries other than Malaysia. Malaysia is a multiracial country which might have different cultural behaviours. This difference might affect the different use of traditional medicines that contributes to supratherapeutic INR.

Objective: This study aimed to determine the prevalence of supratherapeutic INR in warfarin use and its associated factors among the AF patients.

Method: The study population consisted of patients who were diagnosed with AF, treated with warfarin and followed up in the warfarin clinic at Hospital Teluk Intan, Perak. Secondary data was retrieved from retrospective record review in the warfarin clinic at Hospital Teluk Intan, Perak. Logistic regression was used to predict the contributing factors of supratherapeutic INR.

Result: In total, 167 patients were included in the study. Of that, 79 patients (47.3%) were identified to have supratherapeutic INR in which bleeding occurrences happened in 23 patients (29.1%). Patients with heart failure were found to be 2.88 times more likely to develop supratherapeutic INR (OR=2.88; 95% CI: 0.89 to 9.39; p=0.078) than patients without heart failure. Besides, patients who were on regular methyl salicylate cream application were found to have 24.98 times higher risk of developing supratherapeutic INR (OR=24.98; 95% CI: 2.07 to 301.41; p=0.011). Based on HAS_BLED bleeding risk score, AF patients who belong to high-risk group, HAS_BLED score of ≥ 3 , were 36.69 times more prone to supratherapeutic INR than patients who belong to non-high-risk group of HAS_BLED score < 3 (OR=36.69; 95% CI: 12.87 to 104.64; p<0.001).

Conclusion: AF patients with heart failure, HAS_BLED score of ≥ 3 and using methyl salicylate cream should be closely monitored for the potential risk of supratherapeutic INR.

Keywords: INR, supratherapeutic, warfarin

NMRR ID: NMRR-18-2933-44474

Corresponding Author: Loo Sook Peng

Department of Pharmacy, Hospital Teluk Intan, Jalan Changkat Jong, 36000 Teluk Intan, Perak

Email: loosookpeng@moh.gov.my

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, which is characterised by uncoordinated atrial activation with consequent deterioration of atrial mechanical function (1). One of the major clinical complications in AF is systemic and pulmonary embolisation. As a result of embolic risk, chronic oral anticoagulant, for example vitamin K antagonist, warfarin, is recommended for most AF patients to reduce AF related deaths (2). Although warfarin is proven to be an effective anticoagulant, it has a narrow therapeutic range which poses a challenge in the treatment of AF. The international normalised ration (INR), which is derived from the ratio between the actual prothrombin time and that of a standardised control serum, is used as a guide to adjust the doses of warfarin (1).

In the current setting, the therapeutic INR range for AF patients is 2.0-3.0 (3). A meta-analysis by Hart *et al.* (4) revealed that the adjusted dose of warfarin within the therapeutic range of INR (2.0-3.0) showed a significant 64% risk reduction in stroke and 26% reduction of all-cause mortality in patients with non-valvular AF. Supratherapeutic INR in AF is defined as an INR greater than the target range (5). One of the most common adverse reactions of supratherapeutic INR are haemorrhagic incidents. The risk of bleeding was evaluated in a cohort study of over 16,000 patients who have been diagnosed of AF between 2005 and 2010. The incidence of major bleeding with current, recent, past or no warfarin exposure was 3.8, 4.5, 2.7 and 2.9 per 100 patient-years, respectively (6).

In the late 1990s, clinically applicable stroke risk-stratification schemes in AF patients were developed in small cohort studies and had later been refined and validated in larger populations (7-11). The introduction of the CHA₂DS₂-VASc score has simplified the initial decision for oral anticoagulant in AF patients. The HAS-BLED tool was developed to provide a risk score to estimate the 1-year risk for major bleeding (12,13). It is of paramount importance to weigh between the clinical benefits and bleeding risks before initiating warfarin among the AF population. It should be a shared decision making between the physicians and patients on the initiation of warfarin.

A study by McGriff-Lee *et al.* (5) revealed that the prevalence of supratherapeutic INR in AF patients was 39%. This high percentage of supratherapeutic INR urged the researchers to study the prevalence of supratherapeutic INR following warfarin use among the AF patients in Malaysia, which was not available to date. Malaysia is a multiracial country that consists of Malay, Chinese, Indian and other races which might have different cultural behaviours compared to the other countries. Hence, the objective of this study was to determine the prevalence of supratherapeutic INR in warfarin use and its associated factors among AF patients in Hospital Teluk Intan, Perak.

Methodology

This was a retrospective record review using secondary data from the patients' medical records retrieved from the warfarin clinic of Hospital Teluk Intan, Perak. The warfarin clinic in Hospital Teluk Intan is managed by the medical officers and helped by the pharmacists who manage the warfarin Medication Therapy Adherence Clinic (MTAC). One of the main roles of MTAC pharmacists is to provide continuity and enhance patient care through education, monitoring, and close follow-up to patients who require warfarin therapy.

In this study, patients were included if they were treated with warfarin, attended the warfarin clinic in Hospital Teluk Intan from January 2017 to December 2017, started on warfarin for at least six months and older than 18 years old, whereas patients with missing data were excluded. Sample size was calculated using the formula with Finite Population Correction (Daniel WW, 1999), and the minimum number of samples needed to achieve in this study was 149. A standard data collection form was used to collect patients' demographic and clinical data, such as HAS_BLED score category, comorbidities, concurrent medications and use of over-the-counter medication, from the patients' medical records.

The prevalence of supratherapeutic INR events (INR > 3.0) and bleeding occurrences among the included patients from January 2017 to December 2017 were determined. The prevalence of supratherapeutic INR was calculated as the number of patients having at least one episode of supratherapeutic INR over the total number of patients who were included in the study during the one-year study period. Bleeding occurrences were the number (percentage) of patients with supratherapeutic INR who were presented with bleeding episodes.

Descriptive statistics were used to summarise the socio-demographic characteristics of patients. Continuous variables such as age were presented in mean and standard deviation for normally distributed data, or median and interquartile range (Q1, Q3) for data that are not normally distributed. Categorical data (gender, ethnicity, smoking behaviour, alcohol consumption, comorbidities, acute illness/acute infection at the time of supratherapeutic INR and concurrent medications) were presented in frequency and percentage. For the comparison between the two outcome groups (Supratherapeutic INR versus Non Supratherapeutic INR), Chi-square test was used for categorical variables, while t-test was used for continuous variables. A binary logistic regression was performed to analyse factors associated with supratherapeutic INR. Variables with $p < 0.25$ were then included in the multiple logistic regression analysis.

Results

The medical records of a total of 368 patients were screened in the warfarin clinic. We excluded 201 patients who received warfarin for indications other than atrial fibrillation, patients with incomplete data and patients who were lost to follow up. As a result, a total of 167 patients were included in the study. According to the data reported in Table 1, 56.9% of the studied population constituted of male patients, and the ratio of male to female patients was 1.3:1. The mean age of the patients was 65.99 ± 9.12 years.

In this study, 79 patients (47.3%) were reported to have supratherapeutic INR, among which bleeding occurrences were found to happen in 23 patients (29.1%). A total of 65.2% these patients had gum bleeding, 30.4 % had haematuria and 4.3% had haemoptysis. Among the patients with supratherapeutic INR, the proportion between the male and female patients had no significant difference, with 54.4% and 45.6 % respectively. Malay ethnic had the highest percentage of supratherapeutic INR, 63.3% as compared to Chinese ethnic (26.6%) and Indian ethnic (10.1%). As shown in Table 1, variables found to be significantly different between supratherapeutic and non supratherapeutic INR were the HAS_BLED score category ($p < 0.001$), heart failure ($p = 0.033$), chronic kidney disease ($p = 0.033$), and methyl salicylate cream use ($p < 0.001$).

Among the factors analysed for the association with the risk of supratherapeutic INR, as presented in Table 2, smoking status, HAS-BLED score category, heart failure, chronic kidney disease, simvastatin and methyl salicylate cream use ($p < 0.25$) were then subjected for multiple logistic regression. As for the factors of hepatic dysfunction, anemia, acute illness, paracetamol, NSAIDs, Tongkat Ali and ginseng variables, logistic regression analysis was not possibly done due to the lack of exposed patients in either of the comparison groups.

Patients who were on regular methyl salicylate cream application found to have 24.98 times higher odds of developing supratherapeutic INR (OR 24.98; 95% CI 2.07-301.41; $p = 0.011$). Based on HAS_BLED bleeding risk score, AF patients who belong to high risk group, HAS_BLED score ≥ 3 , were 36.69 times more prone to supratherapeutic INR than patients who belong to non-high-risk group, HAS_BLED score of < 3 (OR 36.69; 95% CI 12.87-104.64; $p < 0.001$). Besides, patients with heart failure were found to be 2.88 times more likely to develop supratherapeutic INR (OR 2.88; 95% CI 0.89-9.39; $p = 0.078$) than patients without heart failure.

Table 1: Baseline characteristic and factors associated with supratherapeutic INR in warfarin use among atrial fibrillation patients (n=167)

	Supratherapeutic INR (n=79)	Non Supratherapeutic INR (n=88)	Total (n=167)	p-value
Age, years, mean±SD	67.47±10.18	64.66±9.13	65.99±9.12	0.062*
Gender, n (%)				0.544#
Male	43 (54.4)	52 (59.1)	95 (56.9)	
Female	36 (45.6)	36 (40.9)	72 (43.1)	
Ethnicity, n (%)				0.937#
Malay	50 (63.3)	58 (65.9)	108 (64.7)	
Chinese	21 (26.6)	22 (25.0)	43 (25.7)	
Indian	8 (10.1)	8 (9.1)	16 (9.6)	
Smoking, n (%)				0.441#
Non smoker	64 (81.0)	64 (72.7)	128 (76.6)	
Ex-smoker	7 (8.9)	12 (13.6)	19 (11.4)	
Active smoker	8 (10.1)	12 (13.6)	20 (12.0)	
Duration of smoking, years, mean±SD	31.33±11.87	24.13±12.76	26.97±12.76	0.089*
Number of cigarettes per day, sticks, median (Q ₁ ,Q ₃)	10 (10,10)	10 (5,10)	10 (5,10)	0.789*
Alcohol consumption, n (%)				0.509#
Non alcoholic	77 (97.5)	86 (97.7)	163 (97.6)	
Ex- alcoholic	1 (1.3)	0 (0)	1 (0.6)	
Active alcoholic	1 (1.3)	2 (2.3)	3 (1.8)	
Warfarin starting dose, mg, median (Q ₁ ,Q ₃)	2.5 (2.0,3.0)	3.0 (2.0,4.0)	3.0 (2.0,3.5)	0.498*
Baseline INR, median (Q ₁ ,Q ₃)	1.9 (1.35,2.15)	2.0 (1.35,2.2)	1.97 (1.35,2.19)	0.950*
HAS-BLED score category, n (%)				<0.001# ‡
Low risk	0 (0)	27 (30.7)	27 (16.2)	
Intermediate risk	6 (7.6)	38 (43.2)	44 (26.3)	
High risk	73 (92.4)	23 (26.1)	96 (57.5)	
Comorbidities, n (%)				
Rheumatic heart disease	5 (6.3)	10 (11.4)	15 (8.9)	0.256#
Heart failure	20 (25.3)	11 (12.5)	31 (18.6)	0.033#
Chronic kidney disease	8 (10.1)	8 (10.1)	10 (6.0)	0.033#
Hyperthyroidism	12 (15.2)	10 (11.4)	22 (13.2)	0.465#
Diabetic mellitus	23 (29.1)	21 (23.9)	44 (26.4)	0.442#
Hypertension	71 (89.9)	77 (87.5)	148 (88.6)	0.630#
Ischemic heart disease, n (%)	35 (44.3)	40 (45.5)	75 (44.9)	0.881#
Dyslipidaemia	16 (20.3)	17 (19.3)	33 (19.8)	0.880#
Cerebral vascular accident	18 (19.0)	16 (18.2)	34 (20.4)	0.461#
Concurrent medications, n (%)				
Proton pump inhibitor	7 (8.9)	9 (10.2)	16 (9.6)	0.765#
Ranitidine	20 (25.3)	22 (25.0)	42 (25.2)	0.962#
Simvastatin	55 (69.0)	53 (60.2)	108 (64.7)	0.205#
Antiplatelet	30 (38.0)	28 (31.8)	58 (34.7)	0.404#
Allopurinol	1 (1.3)	3 (3.4)	4 (2.4)	0.366#
Traditional medicines / Supplements / OTC medicines, n (%)				
Paracetamol	16 (20.3)	0 (0)	16 (9.6)	Undefined#
NSAIDs	17 (21.5)	0 (0)	17 (10.2)	Undefined#
Methyl salicylate cream	14 (17.7)	1 (1.3)	15 (9.0)	<0.001#
Tongkat Ali	3 (3.8)	0 (0)	3 (1.8)	Undefined#
Ginseng	3 (3.8)	0 (0)	3 (1.8)	Undefined#

* t-test; # Chi-square test (X^2); ‡ Post hoc bonferroni test were carried out to check on the significance lies among the low-risk, intermediate-risk and high-risk group of HAS_BLED score category. The results shown that there is significant difference between high-risk group and intermediate-risk group ($p<0.001$), and high-risk group and low-risk group ($p<0.001$).

Abbreviation: OTC – over the counter

Table 2: Binary logistic regression and multiple logistic regression analysis on the predictors of supratherapeutic INR among patients with atrial fibrillation (n=167)

Variable	Supratherapeutic INR (n=79)	Non Supratherapeutic INR (n=88)	Crude OR	95% CI	X ² stat. (df)	p-value ^a	AOR	95% CI	X ² stat. (df)	p-value ^a
Age	Not applicable	Not applicable	1.031	0.998,1.065	3.554 (1)	0.064				
Gender										
Male	43	52	1.00							
Female	36	36	1.209	0.655,2.234	0.369 (1)	0.544				
Ethnicity					0.131 (2)	0.937				
Malay	50	58	1.00							
Chinese	21	22	1.107	0.546,2.247	0.080 (1) ^b	0.778 ^b				
Indian	8	8	1.160	0.406,3.316	0.077 (1) ^b	0.782 ^b				
Smoking [¶]										
Non smoker	64	64	1.00							
Smoker	15	24	0.625	0.301,1.300	1.610 (1)	0.208				
Alcoholic [¶]										
Non alcoholic	77	86	1.00							
Alcoholic	2	2	1.117	0.154,8.121	0.012 (1)	0.913				
HAS-BLED score category [¶]										
Non-high-risk	6	65	1.00				1.00			
High-risk	73	23	34.384	13.183,89.768	84.182 (1) ^b	<0.001	36.69	12.87,104.64	45.39 (1) ^b	<0.001^b
Rheumatic heart disease										
Yes	5	10	0.527	0.172,1.615	1.319 (1)	0.251				
No	74	78	1.00							
Heart failure										
Yes	20	11	2.373	1.055,5.335	4.555 (1)	0.033	2.88	0.89,9.39	3.11 (1) ^b	0.078 ^b
No	59	77	1.00				1.00			
Chronic kidney disease										
Yes	8	8	4.845	0.997,23.547	4.805 (1)	0.028				
No	71	80	1.00							
Hyperthyroidism										
Yes	12	10	1.397	0.568,3.438	0.532 (1)	0.466				
No	67	78	1.00							
Diabetic mellitus										
Yes	23	21	0.763	0.383,1.521	0.591 (1)	0.442				
No	56	67	1.00							

Table 2 (continue)

Variable	Supratherapeutic INR (n=79)	Non Supratherapeutic INR (n=88)	Crude OR	95% CI	X ² stat. (df)	p-value ^a	AOR	95% CI	X ² stat. (df)	p-value ^a
Hypertension										
Yes	71	77	1.268	0.482,3.332	0.234 (1)	0.629				
No	8	11	1.00							
Ischemic heart disease										
Yes	35	40	1.048	0.569,1.930	0.022 (1)	0.881				
No	44	48	1.00							
Dyslipidaemia										
Yes	16	17	0.943	0.440,2.021	0.023 (1)	0.880				
No	63	71	1.00							
Cerebral vascular accident										
Yes	18	16	1.328	0.624,2.825	0.543 (1)	0.461				
No	61	72	1.00							
Proton pump inhibitor										
Yes	7	9	0.853	0.302,2.410	0.090 (1)	0.764				
No	72	79	1.00							
Ranitidine										
Yes	20	22	1.017	0.505,2.048	0.002 (1)	0.962				
No	59	66	1.00							
Simvastatin										
Yes	55	53	1.513	0.796,2.876	1.615 (1)	0.204				
No	24	35	1.00							
Antiplatelet										
Yes	30	28	1.312	0.693, 2.484	0.696 (1)	0.404				
No	49	60	1.00							
Allopurinol										
Yes	1	3	0.363	0.037,3.565	0.862 (1)	0.353				
No	78	85	1.00							
Methyl salicylate cream										
Yes	14	1	18.738	2.403,146.149	16.157 (1)	<0.001	24.98	2.07,301.41	6.41 (1) ^b	0.011^b
No	65	87	1.00				1.00			

a Likelihood Ratio (LR) test; b Wald test; ¶ Data is collapsed/merged for binary logistic analysis

Abbreviation: AOR – adjusted odds ratio, OR – odds ratio, CI – confidence interval

Discussion

It is worthwhile to note that the majority of AF patients on warfarin therapy in this study were male, making up 56.9 % of the patients, which is comparable to the similar study conducted by Son *et al.* (14) with 55.7%. Most of the patients included in this study were ranging from 57 to 75 years old, and most of them were non-smokers and non-alcoholics.

Among the comorbidities investigated, hypertension was found to be the most prevalent disease (88.6%) among AF patients. This finding is parallel with the data shown by Data Analytics CMMS 2011 (15), hypertension occupied the first place in the most common chronic comorbid among AF patients, which constituted 83.0% of those older than 65 years old and 81.1% of those younger than 65 years old (15). Hypertension is a strong risk factor for stroke in AF and appeared as an independent risk in CHA₂DS₂-VASc score. Uncontrolled high blood pressure increases the risk of stroke and bleeding events and may lead to recurrent AF. Therefore, good blood pressure control should be an integral part in the management of AF patients.

Most of the patients in this study have other comorbidities besides AF such as hypertension, ischemic heart disease and hyperlipidaemia. They were concurrently prescribed with medications other than warfarin. Precautions must be taken to avoid drug- drug interactions. The most commonly used concurrent medication was simvastatin, followed by antiplatelet, ranitidine and proton pump inhibitors. These results were in concordance with the comorbidities commonly found in the Malaysian population. Lipid lowering agents from the statin group are one of the important drugs used in the management of cardiovascular diseases based on the local and overseas guidelines. According to the Clinical Practice Guidelines Management of Type 2 Diabetes Mellitus (5th Edition) Malaysia, all patients over the age of 40 should be initiated with a statin regardless of the baseline LDL cholesterol level (16). Besides that, therapy with statins in patients with acute ST and non-ST elevation myocardial infarction reduces the rate of recurrent MI, coronary heart disease mortality, need for myocardial revascularization and stroke (17,18).

Pain relief medications were the most commonly used over-the-counter medications among our study population, which included paracetamol, NSAIDs and methyl salicylate cream. Considering that more than 90% of the patients were the elderly above 65 years old, they were inclined to use these medications for fever and pain, particularly NSAIDs and methyl salicylate cream for arthritis pain. To avoid any potential drug interactions with warfarin, extensive counselling should be given to the patients and their caretakers to prevent supratherapeutic INR and subsequently the risk of bleeding.

The prevalence of supratherapeutic INR in this study was 47.3% as compared to the prevalence reported by McGriff-Lee NJ (from the eastern US) (5) which was 39.0%. One of the reasons was the older mean age in the supratherapeutic arm (67.5 years versus 56.0 years) observed in our study. This finding was supported by Fromm *et al.* (19), whereby even after adjustment for other predictive factors, for every 10 years of increase in age, there was a 15% increase in the risk of supratherapeutic INR readings, which warranted a temporary cessation of warfarin therapy. Furthermore, it has been previously shown by Russmann *et al.* (20) that the steady- state warfarin dosage decreases with age and this is mainly due to a significantly reduced metabolic clearance in the elderly patients.

Next, in the present study, 23 patients were reported to have bleeding events. Fang MC *et al.* (21) and Pancholy SB *et al.* (22) in their respective study revealed that there was no gender difference in developing supratherapeutic INR and hence bleeding episodes in warfarin treated AF patients. These findings supported the outcome in the current study, where gender was not a significant factor in predicting the risk for supratherapeutic INR in this study. Smoking affects warfarin metabolism and causes deranged INR readings. In the current study, smokers were found to have a 60% lower risk of experiencing supratherapeutic INR as compared to non-smokers. Although this finding was not statistically significant, it was supported by a meta-analysis by Nathisuwan S *et al.* (23) where the investigators evaluated the effect of chronic cigarette smoking on warfarin metabolism.

Methyl salicylate cream use and HAS_BLEED score category were found to be significantly different between patients with and without supratherapeutic INR. While heart failure is not a significant variable, it is included by the logistic regression because of its significant contribution to the risk of supratherapeutic INR in terms of pathophysiology. Methyl salicylate, an active ingredient in topical analgesic preparations, is commonly prescribed for ameliorating painful musculoskeletal disorders of various aetiologies. It is well known that methyl salicylate cream has drug-drug interaction when used concurrently with warfarin. In concordance with the known interaction, this study revealed that patients who used methyl salicylate cream had 24.98 folds higher odds to obtain at least one supratherapeutic INR. The

interaction between warfarin and methyl salicylate has been studied by Yip *et al.* among eleven patients. The Mean INR of the patients increased from 2.3 to 4.5 after a significant usage of topical methyl salicylate cream, which resulted in a positive alteration of the blood level of salicylate. Researchers postulated that methyl salicylate prolongs INR by depressing prothrombin formation in the liver (24). Also, methyl salicylate is known to be able to inhibit the synthesis of vitamin K-dependent clotting factors, hence displacing warfarin from protein binding sites. It leads to an increase in free drug level, followed by the risk of supratherapeutic INR (25).

In our study, patients who were in the high-risk HAS-BLED score category were found 36.69 times more prone to supratherapeutic INR. The HAS-BLED tool was developed to provide a risk score to estimate the one-year risk of major bleeding. Patients were evaluated based on their clinical characteristics, with the scores ≥ 3 classified as patients with a high risk of bleeding. These characteristics included hypertension (defined as SBP >160 mmHg), abnormal renal function (the presence of chronic dialysis or renal transplantation or serum creatinine ≥ 200 μ mol/L), abnormal liver function (chronic hepatic disease or biochemical evidence of significant hepatic derangement), stroke (previous history of stroke), bleeding, labile INR, elderly (age ≥ 65), drug therapy (concomitant therapy such as antiplatelet agents, NSAIDs) and alcohol intake (consuming ≥ 8 alcoholic drinks per week) (12,13). Gallego *et al.* (26) conducted a prospective study to evaluate the usefulness of the HAS-BLED score in predicting both major bleeding and cardiovascular events in a cohort of anticoagulated patients with AF. Cox regression analysis showed that patients with HAS-BLED score ≥ 3 had a hazard ratio of 3.68 (95% CI 2.37 to 5.78; $p < 0.001$). Nevertheless, cox regression analysis was not possible in the current study due to the absence of mortality data.

Heart failure has been found to interfere with INR stabilisation. Our patients with heart failure had 2.88 times higher odds of experiencing supratherapeutic INR compared to patients without heart failure. Although this is not a statistically significant observation, it is included by the logistic regression because of its significant contribution to the risk of supratherapeutic INR in terms of pathophysiology. This finding is supported by a cohort study by Visser *et al.* (27), which identified heart failure as an independent risk factor for excessive anticoagulation. Heart failure patients had a 1.5-fold to two-fold higher risk of INR >6 . The increase in warfarin responsiveness and sensitivity is assumed to be the result of liver congestion. Both liver congestion and dysfunction are especially prominent during decompensated heart failure and most of the time, they are presented as hepatomegaly. In addition, the study by Hylek *et al.* (28) provided up to date evidence that heart failure exacerbation is associated with increased response to warfarin, by demonstrating a prolonged delay in the return of INR to within the therapeutic range after supratherapeutic INR. This group of researchers suggested oxygen limitation theory to be a plausible mechanism for the effect of heart failure on the excessive response to warfarin (28,29). Phase I drug metabolism by hepatic cytochrome P450 enzymes are directly dependent on oxygen supply. While there is no barrier to oxygen uptake by simple diffusion in the normal liver, in patients with liver impairment, there is reduced oxygen supply to hepatocytes. Therefore, in decompensated heart failure with an oedematous liver, oxygen diffusion to hepatocytes could be impaired, and warfarin metabolism could be reduced (28,29). This will then increase the risk of supratherapeutic INR in warfarin users.

The findings in this study are important to prevent supratherapeutic INR and subsequently haemorrhagic complications, by paying special attention to these risk factors when monitoring warfarin therapy. However, there were a few limitations in the current study. Firstly, the retrospective nature of the study was sensitive to potential human errors in the documentation of the medical records. The prospective exploration of the lifestyle and dietary details of the patients, which is an essential part of supratherapeutic INR assessment, was not possible. Due to the temporal limitation, convenient sampling instead of random sampling was used in this study. Convenient sampling was the contextual ideal choice when it was limited by the short research duration. Also, since the present study only involved a single institution, the results obtained may have limited generalisability to the Malaysian population.

Since AF is a disease with high economic impact and healthcare burden besides affecting the quality of life of the patients, effective management is needed to reduce the morbidity and mortality among AF patients. Therefore, there are some recommendations that can be made from this study. Firstly, the monitoring of time in therapeutic range (TTR) for warfarin should be implemented in the current setting to provide a better insight about the anticoagulation management of warfarin because TTR measures the percentage of time a patient's INR is within the desired treatment range or goal. As the monitoring of TTR is not routinely practised in the warfarin clinic of Hospital Teluk Intan, implementing this practice may better manage the risk of supratherapeutic INR and bleeding occurrences. Besides that, the

small sample size and single-centred design may have resulted in the statistically insignificance of some variables in the logistic regression, for example chronic kidney disease and the use of NSAID, which were demonstrated as the risk factors for supratherapeutic INR in other studies. In view of this, multi-centre study involving more hospitals in Malaysia can be carried out to generate meaningful evidence for the local population. The findings could then be used to create a model to predict the risk of supratherapeutic INR for every AF patient so that patients found to have high risk of supratherapeutic INR can be closely monitored or considered for the use of direct oral anticoagulants.

Conclusion

In this study, the prevalence of supratherapeutic INR was reported to be 47.3% with 29.1% bleeding occurrences. Logistic regression revealed that the factors that contributed to the supratherapeutic INR included HAS_BLED bleeding risk, heart failure and the use of methyl salicylate cream. It is of paramount importance to identify the contributing factors to achieve the goal of therapy in managing over-anticoagulation problems among AF patients treated with warfarin. Patients presented with these three risk factors should be reviewed more often and extensive counselling should be done not only to the patients but also to the caregivers.

Acknowledgement

Deepest gratitude to the Director General of Health Malaysia for his permission to publish the article and Dr Fatimatu Zahra' Abd Aziz and Dr Nur Aizati Athirah Binti Daud for proofreading the manuscript. We are also grateful to Hospital Teluk Intan for the support.

Conflict of Interest Statement

This study was not funded by any party. The authors declared that they have no known competing interests that could have appeared to influence the work reported in this paper.

References

1. Malaysia Clinical Practice Guidelines on Management of Atrial Fibrillation 2012.
2. Hylek EM, Go AS, Chang Y, Jensvold NG, Henault LE, Selby JV, Singer DE. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. *New England Journal of Medicine*. 2003 Sep 11;349(11):1019-26.
3. Malaysia Anticoagulation MTAC(AC-MTAC) Protocol 2nd edition 2020
4. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007;146:857–867.
5. McGriff-Lee NJ, Csako G, Chen JT, Dang DK, Rosenfeld KG, Cannon RO, Macklin LR, Wesley RA. Search for predictors of nontherapeutic INR results with warfarin therapy. *Annals of Pharmacotherapy*. 2005 Dec;39(12):1996-2002.
6. Gallagher AM, van Staa TP, Murray-Thomas T, Schoof N, Clemens A, Ackermann D, Bartels DB. Population-based cohort study of warfarin-treated patients with atrial fibrillation: incidence of cardiovascular and bleeding outcomes. *BMJ open*. 2014 Jan 1;4(1):e003839.
7. The SPAF III Writing Committee for the Stroke Prevention in Atrial Fibrillation Investigators. Patients with nonvalvular atrial fibrillation at low risk of stroke during treatment with aspirin: Stroke Prevention in Atrial Fibrillation III Study. *JAMA* 1998;279:1273–1277.
8. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA* 2001;285:2864–2870.
9. Van Walraven C, Hart RG, Wells GA, Petersen P, Koudstaal PJ, Gullov AL, Hellemons BS, Koefed BG, Laupacis A. A clinical prediction rule to identify patients with atrial fibrillation and a low risk for stroke while taking aspirin. *Arch Intern Med* 2003;163:936– 943.
10. Wang TJ, Massaro JM, Levy D, Vasan RS, Wolf PA, D'Agostino RB, Larson MG, Kannel WB, Benjamin EJ. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community: the Framingham Heart Study. *JAMA* 2003;290:1049–1056.
11. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor- based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137:263–272.
12. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management

- of atrial fibrillation: the Task Force for the Management of Atrial
13. Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010; 19: 2369- 429.
 14. Pisters R, Lane DA, Nieuwlaat R, de Vos CB et al. 2010. A Novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro heart survey. *Chest*. 2010. 138 (5) 1093-1100.
 15. Son MK, Lim NK, Park HY. Trend of prevalence of atrial fibrillation and use of oral anticoagulation therapy in patients with atrial fibrillation in South Korea (2002–2013). *Journal of epidemiology*. 2018 Feb 5;28(2):81-7.
 16. Office of Information Products and Data Analytics CMMS. CMS administrative claims data, January 2011-December 2011, From the Chronic Condition Warehouse.
 17. Clinical Practice Guidelines Management Of Type 2 Diabetes Mellitus (5th Edition) Malaysia.
 18. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, Holmes DR, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN. 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2014 Dec 23;64(24):e139-228.
 19. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio AL, Crea F, Goudevanos JA, Halvorsen S, Hindricks G. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal*. 2017 Aug 26;39(2):119-77.
 20. Fromm P, Miron E, Barak M. Oral anticoagulants in the elderly. *British journal of haematology*. 2003 Feb;120(3):526-8.
 21. Russmann, S., Ggohlke-Barwolf, C., Jahnchen, E., Trenk, D. & Roskamm, H. (1997) Age-dependent differences in the anticoagulant effect of phenprocoumon in patients after heart valve surgery. *European Journal of Clinical Pharmacology*, 52, 31–35.
 22. Fang MC, Singer DE, Chang Y, Hylek EM, Henault LE, Jensvold NG, Go AS. Gender differences in the risk of ischemic stroke and peripheral embolism in atrial fibrillation: the AnTicoagulation and Risk factors In Atrial fibrillation (ATRIA) study. *Circulation*. 2005 Sep 20;112(12):1687-91.
 23. Pancholy SB, Sharma PS, Pancholy DS, Patel TM, Callans DJ, Marchlinski FE. Meta- analysis of gender differences in residual stroke risk and major bleeding in patients with nonvalvular atrial fibrillation treated with oral anticoagulants. *The American journal of cardiology*. 2014 Feb 1;113(3):485-90.
 24. Nathisuwan S, Dilokthornsakul P, Chaiyakunapruk N, Morarai T, Yodting T, Piriyanachanusorn N. Assessing evidence of interaction between smoking and warfarin: a systematic review and meta-analysis. *Chest*. 2011 May 1;139(5):1130-9.
 25. Yip AS, Chow WH, Tai YT, Cheung KL. Adverse effect of topical methyl salicylate ointment on warfarin anticoagulation: an unrecognized potential hazard. *Postgrad Med J*. 1990;66(775):367-369
 26. Joss JD, LeBlond RF. Potentiation of warfarin anticoagulation associated with topical methyl salicylate. *Ann Pharmacother*. 2000;34(6):729-733
 27. Gallego P, Roldán V, Torregrosa JM, Gálvez J, Valdés M, Vicente V, Marín F, Lip GY. Relation of the HAS-BLED bleeding risk score to major bleeding, cardiovascular events, and mortality in anticoagulated patients with atrial fibrillation. *Circulation: Arrhythmia and Electrophysiology*. 2012 Apr;5(2): 312-8
 28. Visser LE, Bleumink GS, Trienekens PH, Vulto AG, Hofman A, Stricker BH. The risk of overanticoagulation in patients with heart failure on coumarin anticoagulants. *British journal of haematology*. 2004 Oct;127(1):85-9.
 29. Hylek EM, Regan S, Go AS, Hughes RA, Singer DE, Skates SJ. Clinical predictors of prolonged delay in return of the international normalized ratio to within the therapeutic range after excessive anticoagulation with warfarin. *Annals of internal medicine*. 2001 Sep 18;135(6):393-400.
 30. Le Counteur DG, McLean AJ. The aging liver. Drug clearance and an oxygen diffusion barrier hypothesis. *Clin Pharmacokinet* 1998;34:359-73.

Depression, Anxiety and Stress (DAS), and Workplace Spirituality among Pharmacists and Pharmacist Assistants in the state of Perlis, Malaysia

Soo Pei Pei¹, Mohd Shainol Azmar Kassim¹, Nur Ainin Aqilah Mohd Rafi², Nursyuhaidah Ramli², Raja Masturah Raja Sulaiman³, Dandaithapani Thyagarajan⁴

¹ Pharmaceutical Services Division, Perlis State Health Department, Ministry of Health Malaysia

² Pharmacy Unit, Kangar Health Clinic, Perlis, Ministry of Health Malaysia

³ Pharmacy Unit, Simpang Empat Health Clinic, Perlis, Ministry of Health Malaysia

⁴ Psychiatric Department, Hospital Tuanku Fauziah, Perlis, Ministry of Health Malaysia

Abstract

Introduction: Depression, anxiety, and stress (DAS) are essential indicators for mental health, affecting our quality of life, productivity, and motivation to work. Workplace spirituality considers the team's sense of community, alignment of organizational values, a sense of contribution to society, enjoyment at work, and opportunities for the inner life, which has recently emerged as a significant component of an organisation.

Objectives: This study aimed to determine the prevalence of DAS and its associations with sociodemographic factors, work-related information, and workplace spirituality among the pharmacists and pharmacist assistants in Perlis.

Methods: A cross-sectional study was carried out for two weeks from 1 June 2019. Data was collected from all pharmacists and pharmacist assistants working in the public or private health settings in Perlis. A self-administered questionnaire was distributed to all respondents. Pearson's chi-square and Fisher's exact tests were used in determining factors associated with DAS.

Results: A total of 238 respondents completed the questionnaire (response rate 95.2%). About 48% of the respondents reported high workplace spirituality. The prevalence of depression, anxiety and stress was 28.2%, 40.8%, and 17.6%, respectively. Age and working years were significantly associated with DAS ($p < 0.05$). Other factors such as employment contract and sleep time were found to be associated with depression. There was also a significant association between employment contract with anxiety. Working hours were significantly associated with stress. Nevertheless, workplace spirituality was not associated with DAS ($p > 0.05$).

Conclusion: Common mental health symptoms experienced by the pharmacy staff in Perlis was anxiety, followed by depression and stress. DAS was significantly associated with age and working years but no association was found between workplace spirituality and DAS. The study's findings suggested for early recognition of DAS and appropriate mental health support for pharmacists and pharmacist assistants at their workplaces.

Keywords: depression, anxiety, stress, workplace spirituality, pharmacy, Malaysia

NMRR ID: NMRR-18-3726-45219

Corresponding Author: Soo Pei Pei

Pharmaceutical Services Division, Perlis State Health Department, 48C, Jalan Raja Syed Alwi, Kampung Guar Syed Alwi, 01000 Kangar, Perlis.

Email: peipeisoo@hotmail.com

Introduction

Mental health is an integral part of health. It is the foundation of overall well-being, ensuring an individual's effective functioning to work productively (1). Mental disorders such as depression, stress, and anxiety (DAS) are essential indicators for mental health. In Malaysia, data from the latest National Health Morbidity Survey showed that 2.3% of Malaysian adults have depression (2). Healthcare workers are among the high-risk population who struggle with mental health disorders as they face enormous pressures in their working environment (3).

Studies related to DAS among healthcare workers in Malaysia are few but increasing in recent years. Khor *et al.* (2017) found that the prevalence of DAS among healthcare professionals (doctors, pharmacists, and nurses) working in the medical wards of Hospital Miri were 40.5%, 66.7%, and 35.7%, respectively (4). In addition, a study conducted among 140 medical officers working in the emergency departments of Malaysian hospitals found that the prevalence of anxiety was 23.8% (5). Another study reported that about three-quarters of nurses working in the public hospitals in Klang Valley expressed emotional distress including DAS (6). Nonetheless, we have little published evidence concerning the emotional distress among pharmacy staff working in Malaysia.

Work and workplace hold a vital role in an individual's life. Workplace spirituality has recently emerged as a significant aspect of an organisation (7). It includes the team's sense of community, alignment of organisational values, a sense of contribution to the society, enjoyment at work, and opportunities for inner life (8). Spirituality at the workplace could contribute to a more effective organisational work process, increase productivity (9) and job satisfaction (7). To date, literature studying the association of workplace spirituality and DAS is relatively scarce.

The high prevalence of mental health problems among the healthcare professionals is a cause for concern because it appears to be affecting the quality, safety and overall healthcare system performance (10). Poor mental health status is also associated with medical errors (11) or decreased performance (12). Hence, early recognition of mental illness among the healthcare professionals is vital to address these problems. The objective of this study was to estimate the prevalence of DAS among the pharmacists and pharmacist assistants working in Perlis. The study also aimed to explore the relationship between DAS and sociodemographic, work-related factors, and workplace spirituality.

Methods

This cross-sectional study was carried out in Perlis, a northern state of Peninsular Malaysia, starting from 1 June 2019 for two weeks. This study was registered with the National Medical Research Register (NMRR-18-3726-45219) and approved by the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia. Approval to conduct this study was also obtained from the hospital director, district health officer, and managers of all community pharmacies.

This study involved all pharmacy staff currently working in Perlis. We included all pharmacists and pharmacist assistants working in both public and private healthcare settings in Perlis, including hospitals, clinics and community pharmacies. Those who were unable to read and write in English were excluded from this study.

A validated self-administered questionnaire was distributed to all respondents in this study. The questionnaire is only available in English. The first part of the questionnaire collected participants' sociodemographic data and work-related information. The second part of the questionnaire measured the workplace spirituality of the study respondents (17 items). It was adapted from a previous study that measured spirituality at the workplace, including the team's sense of community, alignment between organisational and individual values, sense of contribution to the society, enjoyment at work, and opportunities for the inner life (13). The response options in this section were the categories 'Strongly disagree / Disagree / Neutral / Agree / Strongly agree' which corresponded to a score of 1 to 5. A total score of more than 70 was considered as high in workplace spirituality.

The last part of the questionnaire adopted the Depression, Anxiety and Stress Scale (DASS-21), which is a shorter version of the full survey (DASS-42) (14). There were seven items to measure depression, anxiety and stress, respectively. The responses were assigned a score of 0 for 'Did not apply to me at all', 1 for 'Applied to me to some degree, or some of the time', 2 for 'Applied to me to a considerable degree, or a good part of the time', and 3 for 'Applied to me very much or most of the time'. The total raw score for each DAS component was then multiplied by two to fit with the DASS-42. According to the recommended cut-off, DAS was then dichotomised into two categories, i.e., with or without symptoms. Subjects were categorised as having depression, anxiety, and stress symptoms if each individual score was more than 9, 7 and 14, respectively.

Prior to data collection, the questionnaire was tested for content and face validation. Content validation was carried out by five elected senior pharmacists with at least five years of working experience in consensus until no further correction. Then, face validity was tested against six other pharmacists and pharmacist assistants to ensure the clarity and comprehensibility of the questionnaire.

Three investigators conducted participant recruitment in this study. The list of all pharmacy staff working in Perlis was gathered from credible sources, i.e., the Perlis Health Department database, representatives of the private hospital, and community pharmacies across Perlis. Scheduled appointments were made to each facility for data collection. During each visit, all eligible participants were adequately briefed on the study, and they were allowed to ask any questions if they required further clarification. A paper-based questionnaire was handed to only consented individuals, and they were given approximately 15 to 20 minutes to complete the questionnaire. Completed questionnaires were systematically collected throughout the study, and all responses were assured of anonymity to protect data confidentiality.

Data analyses were carried out using the Statistical Packages for Social Sciences (SPSS) Software Version 20.0. Descriptive analyses on the sociodemographic characteristics, work-related information, workplace spirituality and DAS were performed. Then, Pearson's Chi-square and Fisher's exact test were used to determine the associations of sociodemographic characteristics, work-related information and workplace spirituality with DAS. All statistical tests were performed at a 5% significance level.

Results

Sociodemographic characteristics and work-related information

Of 250 questionnaires distributed during the study, 238 were completed and returned to the investigators, giving a response rate of 95.2%. Respondents' sociodemographic data and work-related information were shown in Table 1. Slightly more than half of the respondents were aged below 30 years old (n=131, 55.0%). The majority were female (n=190, 79.8%). A total of 151 respondents were pharmacists, and 87 were pharmacist assistants. Most of them were public servants (n=175, 73.5%), while the rest were working in the private sector. Of those, more than three-quarters were permanent staff, while 57 respondents (23.9%) were under a fixed-term contract. More than half of the respondents (63.4%) worked for more than three years in the health sector with an average monthly income between RM3000-RM5000 (50.4%).

Workplace spirituality

The results for spirituality among the pharmacists and pharmacist assistants at the workplace were shown in Table 2. Regarding the team's sense of community, 70.1% of the respondents agree that they worked in a team that feels like a family. About 80% of the total respondents think that their team members support and care about each other. When concern about the alignment between organizational and individual values, 68.9% of the respondents felt positive about the workplace's values, 63.8% reported they felt good about their future with the organization. Besides, most of the pharmacy staff agreed that their organisation respects their inner life. For the sense of contribution to the community, more than three-quarters of the respondents reported their work is connected to what they think is essential in life. Most of them agreed that there is a connection between their work and the community, and their work helps the society. Only 12 (5.1%) of the study respondents expressed that they experienced no joy in their work. About 63% reported they feel pleasure when coming to work. In the opportunity for the inner life domain, more than half of the respondents stated their spiritual values are valued in their workplace, and there is room for their spirituality. Among the respondents, 114 (47.9%) of them reported high workplace spirituality.

Depression, Anxiety and Stress (DAS)

Table 3 showed the emotional syndromes of DAS among the pharmacists and pharmacist assistants. For depression, about 42.0% of the respondents reported that they couldn't experience a positive feeling. A total of 54.6% of pharmacy staff said it was difficult to work up the initiative to work. About 60% of them stated the sense of downhearted and blue and unable to become enthusiastic about anything. Regarding anxiety, 32.4% of the respondents experienced difficulty in breathing. About one-third of the respondents felt panic, and 29.4% reported that they felt scared without any good reason. In the last component (stress), more than half of the respondents found it hard to wind down, and they tended to overreact to situations. A total of 37.4% of them reported getting agitated, and 43.3% of them found it difficult to relax. About 42% of respondents said they were intolerant of anything that kept them from getting on with what they were doing. The subscale score of participants for DAS was presented in Table 4. Overall, 67 (28.2%), 97 (40.8%) and 42 (17.6%) had symptoms of depression, anxiety and stress respectively.

Association between sociodemographic factors, work-related information and workplace spirituality with DAS

Table 5 summarised the results of bivariate analyses to explore the relationship between each factor with DAS. There were four factors, including age, employment contract, working years, and sleeping time, that were significantly associated with depression. Pharmacy staff aged 30 years and above had 2.04 times odds (95% CI 1.27-5.26; $p=0.019$) of developing depression symptoms than those below 30 years old. Those working on fixed-term contracts had more odds of developing depression than full-time pharmacy staff (OR=2.86; 95% CI 2.54-3.18; $p=0.003$). The odds of respondents with more than three years of working experience developing depression was 2.12 times odds compared to those working three years or below (95% CI 1.32-5.56; $p=0.011$). Sleeping time was also significantly associated with depression (OR=2.09; 95% CI 1.77-2.41; $p=0.020$).

When concerned about anxiety, three factors (age, employment contract, and working years) were significantly associated with anxiety among the pharmacists and pharmacist assistants working in Perlis. Like depression, pharmacy staff aged 30 years and above were more likely to develop anxiety than their counterparts (OR=2.14; 95% CI 1.87-2.41; $p=0.005$). Respondents with fixed-term contracts had 52% lower odds of developing anxiety than those working on a full-time basis (OR=0.48, 95% CI 0.17-0.79; $p=0.034$). Pharmacists and pharmacist assistants with working experience of more than three years had 2.56 times odds of developing anxiety than their counterparts (95% CI 2.28-2.84; $p=0.001$).

There were three factors that were significantly associated with stress in this study. Pharmacy staff aged 30 and above had 2.35 times odds (95% CI 1.98-2.67; $p=0.019$) of developing stress compared to the younger staff. Those with working experience of more than three years were less likely to have stress than their counterparts (OR=0.40; 95% CI 0.28-0.52; $p=0.007$). Besides, respondents with working hours more than eight hours had 2.02 times odds (95% CI 1.67-2.37; $p=0.042$) of developing stress compared to those who work less than or equivalent to eight hours. Nonetheless, the current study found no significant association between workplace spirituality with DAS ($p>0.05$).

Table 1. Sociodemographic characteristics and work-related information of the respondents (n=238)

Characteristics	n (%)
Age (years)	
<30	131 (55.0)
≥30	107 (45.0)
Gender	
Male	48 (20.2)
Female	190 (79.8)
Marital Status	
Single / Divorced	108 (45.4)
Married	130 (54.6)
No. of Children	
0	127 (53.4)
≥1	111 (46.6)
Races	
Malay	207 (87.0)
Non-Malay	31 (13.0)
Education level	
Diploma	81 (34.0)
Degree and above	157 (66.0)
Occupation	
Pharmacist	151 (63.4)
Pharmacist assistant	87 (36.6)
Workplace	
Public sector	175 (73.5)
Private sector	63 (26.5)
Employment contract	
Full-time contract	181 (76.1)
Fixed term contract	57 (23.9)
Monthly Income (RM)	
<3000	53 (22.3)
3000 - 5000	120 (50.4)
>5000	65 (27.3)
Working years	
≤3	87 (36.6)
>3	151 (63.4)
Working hours/day	
≤8	167 (70.2)
>8	71 (29.8)
Sleeping time/day (hours)	
≤6	150 (63.0)
>6	88 (37.0)

Table 2: Workplace spirituality among the pharmacists and pharmacist assistants in Perlis (n=238)

No.	Questions	n (%)				
		Strongly disagree	Disagree	Neutral	Agree	Strongly agree
Team's sense of community						
1	People in my team feel as if they were part of a family	3 (1.3)	9 (3.8)	59 (24.8)	120 (50.4)	47 (19.7)
2	My team promotes the creation of a spirit of community	2 (0.8)	8 (3.4)	53 (22.3)	131 (55.0)	44 (18.5)
3	I feel that the members of my team/group support each other	2 (0.8)	8 (3.4)	42 (17.6)	127 (53.4)	59 (24.8)
4	I feel that the members of my team/group care about each other	2 (0.8)	8 (3.4)	45 (18.9)	129 (54.2)	54 (22.7)
5	I feel that the members of my team/group are linked by a common purpose	2 (0.8)	7 (2.9)	52 (21.8)	123 (51.7)	54 (22.7)
Alignment between organizational and individual values						
6	I feel positive about the values prevailing in my organization	2 (0.8)	7 (2.9)	65 (27.3)	124 (52.1)	40 (16.8)
7	People feel good about their future with the organization	3 (1.3)	10 (4.2)	73 (30.7)	102 (50.4)	32 (13.4)
8	My organization respects my "inner life"	6 (2.5)	8 (3.4)	69 (29.0)	113 (47.5)	42 (17.6)
9	My organization helps me to live in peace/harmony with myself	6 (2.5)	7 (2.9)	77 (32.4)	108 (45.4)	40 (16.8)
10	The leaders of my organization try to be helpful to the larger social good of the community	4 (1.7)	6 (2.5)	63 (26.5)	118 (49.6)	47 (19.7)
Sense of contribution to the community						
11	My work is connected with what I think is important in life	3 (1.3)	6 (2.5)	47 (19.7)	122 (51.3)	60 (25.2)
12	I see a connection between my work and the larger social good of my community	2 (0.8)	3 (1.3)	44 (18.5)	132 (55.5)	57 (23.9)
13	When working, I feel helpful for the whole society	5 (2.1)	0 (0)	36 (15.1)	121 (50.8)	76 (31.9)
Sense of enjoyment at work						
14	I experience joy in my work	4 (1.7)	8 (3.4)	58 (24.4)	118 (49.6)	50 (21.0)
15	Most days, I feel joy when coming to work	8 (3.4)	15 (6.3)	65 (27.3)	110 (46.2)	40 (16.8)
Opportunities for the inner life						
16	My spiritual values are not valued in my workplace	54 (22.7)	78 (32.8)	64 (26.9)	26 (10.9)	16 (6.7)
17	In my workplace, there is no room for my spirituality	56 (23.5)	85 (35.7)	57 (23.9)	25 (10.5)	15 (6.3)

Table 3: Assessment of depression, anxiety and stress among the pharmacists and pharmacist assistants in Perlis (n=238)

No.	Questions	n (%)			
		Did not apply to me at all	Applied to me to some degree	Applied to me to a considerable degree	Applied to me very much
Depression					
1	I couldn't seem to experience any positive feeling at all	138 (58.0)	72 (30.3)	17 (7.1)	11 (4.6)
2	I found it difficult to work up the initiative to do things	108 (45.4)	99 (41.6)	27 (11.3)	4 (1.7)
3	I felt that I had nothing to look forward to	170 (71.4)	46 (19.3)	12 (5.0)	10 (4.2)
4	I felt downhearted and blue	145 (60.9)	70 (29.4)	17 (7.1)	6 (2.5)
5	I was unable to become enthusiastic about anything	140 (58.8)	75 (31.5)	17 (7.1)	6 (2.5)
6	I felt I wasn't worth much as a person	179 (75.2)	39 (16.4)	12 (5.0)	8 (3.4)
7	I felt that life was meaningless	197 (82.8)	26 (10.9)	7 (2.9)	8 (3.4)
Anxiety					
8	I was aware of dryness of my mouth	115 (48.3)	73 (30.7)	29 (12.2)	21 (8.8)
9	I experienced breathing difficulty (e.g., excessively rapid breathing, breathlessness in the absence of physical exertion)	161 (67.6)	61 (25.6)	10 (4.2)	6 (2.5)
10	I experienced trembling (e.g., in the hands)	159 (66.8)	60 (25.2)	13 (5.5)	6 (2.5)
11	I was worried about situations in which I might panic and make a fool of myself	118 (49.6)	88 (37.0)	19 (8.0)	13 (5.5)
12	I felt I was close to panic	154 (64.7)	65 (27.3)	13 (5.5)	6 (2.6)
13	I was aware of the action of my heart in the absence of physical exertion (e.g., sense of heart rate increase, heart missing a beat)	139 (58.4)	70 (29.4)	16 (6.7)	13 (5.5)
14	I felt scared without any good reason	168 (70.6)	47 (19.7)	14 (5.9)	9 (3.8)
Stress					
15	I found it hard to wind down	97 (40.8)	104 (43.7)	28 (11.8)	9 (3.8)
16	I tended to over-react to situations	103 (43.3)	103 (43.3)	25 (10.5)	7 (2.9)
17	I felt that I was using a lot of nervous energy	129 (54.2)	75 (31.5)	23 (9.7)	11 (4.6)
18	I found myself getting agitated	149 (62.6)	75 (31.5)	8 (3.4)	6 (2.5)
19	I found it difficult to relax	135 (56.7)	85 (35.7)	13 (5.5)	5 (2.1)
20	I was intolerant of anything that kept me from getting on with what I was doing	138 (58.0)	83 (34.9)	11 (4.6)	6 (2.5)
21	I felt that I was rather touchy	103 (43.3)	104 (43.7)	26 (10.9)	5 (2.1)

Table 4: Prevalence of DAS among pharmacists and pharmacist assistants in Perlis (n=238)

	With symptom	Without symptom
Depression	171 (71.8%)	67 (28.2%)
Anxiety	141 (59.2%)	97 (40.8%)
Stress	196 (82.4%)	42 (17.6%)

*The cut-off score for depression, anxiety, and stress were ≥ 10 , ≥ 8 , and ≥ 15 , respectively.

Table 5: Association between sociodemographic factors, work-related information, and workplace spirituality with DAS

Variable	Depression		Anxiety		Stress	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age						
<30 (R)	2.04 [#]	0.019*	2.14 [#]	0.005*	2.35 [§]	0.019*
≥30	(1.27, 5.26)		(1.87, 2.41)		(1.98, 2.67)	
Gender						
Male (R)	1.04 [#]	0.219	1.14 [#]	0.105	1.35 [#]	0.079
Female	(0.87, 3.22)		(0.77, 2.41)		(0.98, 2.47)	
Marital Status						
Single / Divorced	0.74 [#]	0.132	1.72 [#]	0.070	1.48 [§]	0.096
Married (R)	(0.40, 1.22)		(0.76, 2.16)		(0.95, 2.35)	
No. of Children						
0 (R)	0.59 [#]	0.062	2.24 [#]	0.075	1.03 [§]	0.126
≥1	(0.23, 1.02)		(0.96, 3.16)		(0.72, 3.56)	
Races						
Malay	3.04 [#]	0.219	2.41 [#]	0.105	0.69 [§]	0.109
Non-Malay (R)	(0.27, 5.26)		(1.17, 4.21)		(0.27, 1.97)	
Education level						
Diploma (R)	0.99 [#]	0.142	1.24 [#]	0.251	1.54 [§]	0.171
Degree and above	(0.43, 1.22)		(0.96, 2.71)		(0.92, 3.81)	
Occupation						
Pharmacist (R)	0.87 [#]	0.211	1.51 [#]	0.357	2.15 [#]	0.187
Pharmacist assistant	(0.13, 1.22)		(0.71, 3.40)		(0.83, 4.11)	
Workplace						
Public sector	2.10 [#]	0.510	2.22 [#]	0.289	1.15 [#]	0.141
Private sector (R)	(0.40, 4.22)		(0.91, 4.31)		(0.53, 2.17)	
Employment contract						
Full-time (R)	2.86 [#]	0.003*	0.48 [#]	0.034*	1.34 [§]	0.122
Fixed term contract	(2.54, 3.18)		(0.17, 0.79)		(0.81, 2.51)	
Monthly Income						
<RM5000	3.05 [#]	0.222	1.15 [#]	0.074	2.31 [§]	0.157
>RM5000 (R)	(0.81, 5.23)		(0.77, 3.82)		(0.81, 3.58)	
Working years						
≤3 (R)	2.12 [#]	0.011*	2.56 [#]	0.001*	0.40 [§]	0.007*
>3	(1.32, 5.56)		(2.28, 2.84)		(0.28, 0.52)	
Working hours/day						
≤8 (R)	1.23 [#]	0.281	1.19 [#]	0.112	2.02 [#]	0.042*
>8	(0.71, 2.33)		(0.33, 2.27)		(1.67, 2.37)	
Sleeping time/day (hours)						
≤6	2.09 [#]	0.020*	0.88 [#]	0.185	1.34 [§]	0.161
>6 (R)	(1.77, 2.41)		(0.53, 1.96)		(0.62, 2.51)	
Workplace spirituality						
Low	1.35 [#]	0.305	2.71 [#]	0.280	1.35 [#]	0.132
High (R)	(0.80, 3.72)		(0.71, 3.31)		(0.73, 2.56)	

(R) – reference group; OR – odds ratio; 95% CI – 95% confidence interval; [#] Pearson’s chi-square; [§] Fisher exact test; * statistically significant at $p < 0.05$.

Discussion

Despite its evident importance in assessing healthcare workers’ psychological status, the literature on DAS among pharmacists and pharmacist assistants in Malaysia was relatively scarce. Most of the available studies were conducted among the pharmacy students (15,16). In this study, the prevalence of depression, anxiety and stress was 28.2%, 40.8%, and 17.6%, respectively. The psychological distress trend was similar to the results of a study conducted among emergency medical officers in Malaysian hospitals, which showed that anxiety was in the highest percentage, followed by depression and stress (5).

There was a significant association between age with DAS among the pharmacy staff working in Perlis in the current study. It was demonstrated that older staff had more odds of developing DAS compared to younger adults. A similar finding was observed in two other studies in which older adults were associated with DAS compared to different age groups. The studies showed that the elderly were more vulnerable to stress and depression than other ages due to increasing stressors resulting from declining health and

dwindling social relationships (17,18). One of the study revealed that gender was associated with anxiety (18). However, our study showed no association between gender and DAS among the pharmacy staff.

The current study found that employment contracts and working years were associated with depression and anxiety. Consistent with a study conducted in Japan, the employment contract was associated with the workers' psychological health, especially depression (19). In our study, pharmacy staff with fixed-term contracts were more susceptible to develop depression compared to those with a full-time contract. Studies consistently showed that temporary workers experience more job insecurity than permanent workers. There was also growing evidence indicating that job insecurity was one of the most common sources of depression among the contract workers (20). Nevertheless, the present study found that those with fixed-term contracts were less likely to develop anxiety than full-time pharmacy staff.

In contrast to a study conducted in Klang Valley, Malaysia which found that increased working experience was associated with decreased depression level, the current study found that those with more working years were associated with a higher risk of depression and anxiety (6). Pharmacy staff with more working years may need to bear a greater responsibility for their task and duties to achieve their work-related targets, which could lead to depression and anxiety. Several other studies, on the other hand, showed that working experience was not associated with depression, anxiety and stress (4, 5). Besides that, this study showed that long working hours had a significant association with stress levels. The finding was consistent with a study conducted by Yang *et al.* (2017) which found that higher average working hours were related to higher stress levels (4). Long working hours negatively impact work performance, leading to poor decision-making, fatigue, and emotional distress.

Apart from age, employment contract and working years, our study showed that shorter sleep time was associated with depression. Similarly, a study stated that sleep deprivation was associated with depression since sleep is essential for individuals to recover physically and emotionally (21). Sleep deprivation weakens the ability to control emotions, which results in bad moods, negative thinking, and decreased empathy.

Our study found no association between workplace spirituality and depression, anxiety and stress among the pharmacy staff working in Perlis. There was a lack of literature studying the association between workplace spirituality and DAS. Most of the available studies on workplace spirituality were conducted to look at its association with job satisfaction (7), employee productivity (9), and organisation commitment (8). There was also very scarce evidence to substantiate the effects of certain spiritual activities on the overall mental health.

The main limitation in this study was that the results were analysed using bivariate analysis. Further downstream analysis, such as multiple logistic regression, may be used to account for other confounding factors while examining the association between sociodemographic and work-related factors with DAS. Besides that, the findings of this study were limited only to pharmacy staff working in Perlis as concerns about the results' generalisability to the entire population may arise. Future studies may be carried out on a larger scale involving more states across Malaysia.

Conclusion

In conclusion, anxiety was found to be the most common symptom experienced by pharmacy staff in Perlis, followed by depression and stress. Age and working experience were factors associated with DAS. Attention should be focused on early recognition of DAS among the healthcare professionals and specific strategies to address the psychological distress because poor mental health status among healthcare workers could directly affect the work quality, safety and the entire healthcare system.

Acknowledgement

The authors would like to thank the Director General of Health for the permission to publish this study. The authors would also like to thank Mr Ng Yit Han for his advice on data analysis for this study

Conflict of Interest Statement

No external funding was received for this study. The authors declared no potential conflict of interest.

References

1. World Health Organization. Atlas of mental health resources in the world 2001. Available from: <https://apps.who.int/iris/handle/10665/66910>
2. Institute for Public Health. National Health and Morbidity Survey (NHMS) 2019: Non-communicable diseases, healthcare demand, and health literacy-Key Findings. 2020.
3. Kim M-S, Kim T, Lee D, Yook J-h, Hong Y-C, Lee S-Y, et al. Mental disorders among workers in the healthcare industry: 2014 national health insurance data. *Annals of occupational and environmental medicine*. 2018;30(1):1-8.
4. Yang KW, Lee MTL, Ahmad K. Depression, anxiety and stress among healthcare professionals (DASHCP): A cross sectional study.
5. Yahaya SN, Wahab SFA, Yusoff MSB, Yasin MAM, Rahman MAA. Prevalence and associated factors of stress, anxiety and depression among emergency medical officers in Malaysian hospitals. *World journal of emergency medicine*. 2018;9(3):178.
6. Amin NA, Quek KF, Oxley JA, Noah R, Nordin R. Emotional Distress as a Predictor of Work-Related Musculoskeletal Disorders in Malaysian Nursing Professionals. *The international journal of occupational and environmental medicine*. 2018;9(2):69.
7. Fatima T, Naz A, Chughtai S, Khawaja KF. Workplace spirituality and job satisfaction: Moderating role of intrinsic and extrinsic values. *Paradigms*. 2017;11(1):58.
8. Rego A, e Cunha MP. Workplace spirituality and organizational commitment: an empirical study. *Journal of organizational change management*. 2008.
9. Biswakarma G. Impact of workplace spirituality on employee productivity in Nepalese hospitality organizations. *Journal of Tourism and Hospitality Education*. 2018;8:62-76.
10. Dyrbye LN, Shanafelt TD, Sinsky CA, Cipriano PF, Bhatt J, Ommaya A, et al. Burnout among health care professionals: a call to explore and address this underrecognized threat to safe, high-quality care. *NAM perspectives*. 2017.
11. Suzuki K, Ohida T, Kaneita Y, Yokoyama E, Miyake T, Harano S, et al. Mental health status, shift work, and occupational accidents among hospital nurses in Japan. *Journal of occupational health*. 2004;46(6):448-54.
12. Schwenk TL, Gorenflo DW, Leja LM. A survey on the impact of being depressed on the professional status and mental health care of physicians. *The Journal of clinical psychiatry*. 2008;69(4):617-20.
13. Campbell JK, Hwa YS. Workplace spirituality and organizational commitment influence on job performance among academic staff. *Jurnal Pengurusan (UKM Journal of Management)*. 2014;40.
14. Lovibond, SH. & Lovibond, PF. *Manual for the Depression Anxiety Stress Scales*. 2nd Ed. Sydney: Psychology Foundation; 1995.
15. Radeef AS, Faisal GG. Depression, Anxiety and Stress Among Pharmacy Students in Malaysia. *Journal of International Dental and Medical Research*. 2020;13(2):628-32.
16. Yusof NSM, Zainal ZA, Huri HZ, Jacob SA, Alwi MNM, Hassan Y, et al. Prevalence of Depression among Undergraduate Pharmacy Students in Malaysia. *International Journal of Pharmaceutical Research*. 2020;12(3).
17. Mirzaei M, Ardekani SMY, Mirzaei M, Dehghani A. Prevalence of depression, anxiety and stress among adult population: results of Yazd Health Study. *Iranian journal of psychiatry*. 2019;14(2):137.
18. Mohammadi M-R, Davidian H, Noorbala AA, Malekafzali H, Naghavi HR, Pouretamad HR, et al. An epidemiological survey of psychiatric disorders in Iran. *Clinical practice and epidemiology in mental health*. 2005;1(1):1-8.
19. Kompier M, Ybema JF, Janssen J, Taris T. Employment contracts: cross-sectional and longitudinal relations with quality of working life, health and well-being. *Journal of occupational health*. 2009;0903130062.
20. Boya FÖ, Demiral Y, Ergör A, AKVARDAR Y, De Witte H. Effects of perceived job insecurity on perceived anxiety and depression in nurses. *Industrial Health*. 2008;46(6):613-619.
21. Tsuno N, Besset A, Ritchie K. Sleep and depression. *The Journal of clinical psychiatry*. 2005;66(10):1254-69.

Perceptions of Type 2 Diabetes Mellitus Patients towards Insulin Therapy and Willingness to Accept Insulin Therapy at the Public Health Clinics in South Seberang Perai District, Malaysia

Balamurugan Supparamaniam¹, Norul Adlin Abu Safran², Nor Hidayah Ruzalle², Loh Yi Song², Asiah Idris³, Lee Li San¹, Teoh Hui Pin⁴, Teng Jie Ying⁵

¹ Seberang Jaya Hospital, Penang, Ministry of Health Malaysia

² Bukit Panchor Health Clinic, Penang, Ministry of Health Malaysia

³ Sungai Acheh Health Clinic, Penang, Ministry of Health Malaysia

⁴ Jalan Macalister Health Clinic, Penang, Ministry of Health Malaysia

⁵ Pulau Pinang Hospital, Penang, Ministry of Health Malaysia

Abstract

Introduction: Many patients living with Type 2 diabetes mellitus (T2DM) require insulin as an adjunct to lifestyle interventions and oral hypoglycaemic agent (OHA), Timely initiation of insulin therapy at an earlier stage plays a vital role in managing T2DM effectively. Insulin initiation is often delayed due to the refusal of insulin therapy by diabetes patients.

Objective: This study was conducted to evaluate T2DM patients' perceptions towards insulin and willingness to accept insulin therapy, and to identify the associating factors affecting patients' willingness to accept insulin therapy.

Methods: A cross-sectional survey was conducted from 1 January 2018 to 30 April 2018 in four public health clinics of South Seberang Perai District. Validated questionnaires were adopted as the survey tool. Purposive sampling method was used to include insulin naive adult T2DM patients who were on follow-up treatment at the health clinics and were treated with at least one OHA.

Results: A total of 458 patients participated in this survey, among which 338 (73.8%) patients were not willing to accept insulin if initiated. Multiple Logistic Regression showed that females (AOR 1.67, 95% CI 1.09-2.56, $p=0.018$), patients who did not know anybody on insulin (AOR 1.78, 95% CI 1.16-2.75, $p=0.008$) and patients who were not recommended insulin by doctor (AOR 1.83, 95% CI 1.08-3.09, $p=0.024$) more likely to refuse insulin therapy. In terms of perception, patients who felt that taking insulin would make their life less flexible (AOR 2.43, 95% CI 1.49-3.96, $p<0.001$), patients who worry that injecting insulin would be painful (AOR 1.95, 95% CI 1.17-3.24, $p=0.010$), and patients who lacked the confidence to manage insulin therapy (AOR 1.79, 95% CI 1.11-2.90, $p=0.017$) were more likely to refuse insulin.

Conclusions: Current acceptance rate for insulin treatment was only 26.2%. Promoting custom-made patient-centric approach will improve patient's initial negative perception towards accepting insulin therapy.

Keywords: diabetes, insulin, type 2 diabetes melitus

NMRR ID: NMRR-17-1964-37319

Corresponding Author: Balamurugan Supparamaniam

Department of Pharmacy, Hospital Seberang Jaya, Jalan Tun Hussein Onn, 13700 Seberang Jaya, Pulau Pinang.

Email: bala5661@gmail.com

Introduction

Type 2 diabetes mellitus (T2DM) is an endocrine disorder that is characterised by insufficient insulin production or failure of the body to utilise the produced insulin. Almost 150 million people are affected globally (1), and the disease is more prevalent in Asian countries due to poor living standards, inadequate healthcare facilities and demographic shift to aging population (2). T2DM affects almost 21% of Malaysian adults above the age of 30 and has become a major public healthcare concern according to the National

Health and Morbidity Survey 2015. Of the 1.1 million T2DM patients receiving treatment at public healthcare facilities in Malaysia, 70% attended the primary care clinics (3). This shows that primary care is the centre point for diabetes management.

Many patients living with T2DM require insulin as an adjunct to lifestyle interventions and oral hypoglycaemic agent (OHA). While insulin therapy was traditionally managed by specialised diabetes services, it is now largely managed by the primary care teams. Timely initiation of insulin therapy at an earlier stage plays a vital role in managing T2DM effectively. Despite the importance and promising effects of insulin therapy, insulin initiation is often delayed due to the refusal of insulin therapy by diabetic patients (4). Psychological insulin resistance is common among T2DM patients. The resistance is multifactorial but mainly involves negative beliefs and perception regarding diabetes and insulin (5-7). A recent review of 34 studies within the context of primary care (5) supported that insulin-related beliefs, social influences and psychological factors are the main factors contributing to the sub-optimal insulin. However, the review solely involved qualitative studies, and had only included one Malaysian study that focused on the barriers and facilitators of blood glucose in people with type 2 diabetes using insulin (8). There were other prior studies that were conducted in the primary care settings in Malaysia but mostly were on insulin therapy refusal (8,9). Due to the limited number of studies on the perception and willingness to accept insulin therapy, our understanding about the issue is still unclear. The assessment of insulin perception in patients is therefore of vital importance as it has been postulated that the knowledge and perception of patients towards their illness strongly influence their compliance to the prescribed treatment (10). This study was conducted to evaluate the perception towards insulin and willingness to accept insulin therapy among T2DM patients at the primary healthcare setting in Penang, Malaysia. The study also aimed to identify the associating factors affecting patients' willingness to accept insulin therapy.

Methods

This cross-sectional survey was conducted in four public health clinics in the South Seberang Perai District of Penang from 1 January 2018 to 30 April 2018. The clinics were Bandar Tasek Mutiara Health Clinic, Nibong Tebal Health Clinic, Bukit Panchor Health Clinic and Sungai Acheh Health Clinic.

The sample size was determined based on the estimation of 20% dropout, with 95% confidence interval and 5% precision (11). The calculated sample size was 450 respondents. The inclusion criteria for this study were T2DM patients on follow-up treatment at the health clinics aged 18 years and above, who were treated with at least one OHA and being insulin naive. Patients suffering from dementia, cognitive impairment and psychiatric disorder, patients with visual or manual dexterity impairment that would impede self-injection and patients with cerebrovascular accident (CVA) were excluded from this study. Before participating in this study, a written consent was obtained.

Data was collected using a validated questionnaire in English and Malay language. The English version of questions were adopted from Polonsky *et al.* (6) while the translated Malay version of the questionnaire was adopted from Zainuddin *et al.* who conducted a study on psychological insulin resistance (PIR) among T2DM patients (8). The questionnaire consisted of two parts. The first section of the questionnaire collected socio-demographic and clinical information relating to age, gender, ethnicity, educational attainment, occupations, duration of disease, fasting blood glucose level, HbA1c, know relative or friends using insulin, taking traditional and complementary medicines and whether insulin was ever recommended by their physician. The second part of the questionnaire had nine items regarding the perception of patients towards insulin therapy. Each question had a response of either agree or disagree. The patients need to choose one option for each question. The questionnaires were self-administered by the patients and patients took an average of 20 minutes to complete the questions.

Data analyses were conducted using Statistical Package for Social Sciences (SPSS) v.20 (IBM Corp, Armonk, NY, USA.). Continuous values are expressed as the mean \pm standard deviation (SD), and categorical variables are presented as numbers (percentage). The association between risk factors and patient willingness to accept insulin were estimated using univariate analysis and multiple logistic regression. Significant variables in the univariate analysis was included in the multiple logistic regression. The odds ratios and 95% confidence intervals (CI) were estimated, and the level of significance was set at $p < 0.05$.

The ethical approval for this study was obtained from the Medical Research Ethics Committee (MREC), Ministry of Health Malaysia and was registered under National Medical Research Registry (NMRR-17-1964-37319).

Results

A total of 458 respondents participated in the survey with participants' age ranging from 24 to 86 years old. The average mean \pm SD age was 56.7 ± 10.9 years old. The male and female respondents were almost equally distributed and most patients were Malay (44.1%). Most of the respondents in this study did not take any traditional and complementary medicines for their diabetes treatment (86.2%). The mean duration of diabetes was 5.6 years and the mean HbA1C level was 7.8%. Only 120 (26.2%) patients were willing to accept insulin treatment if initiated by their doctor (Table 1).

The perception of study participants towards insulin therapy were presented in Table 2. Almost half (42.8%) of the study respondents agreed that taking insulin could indicate that their disease had become worse, although the majority (82.5%) disagreed that taking insulin can cause problems. On the expected pain, three-quarter (72.5%) agreed that injecting insulin would be painful and more than half (61.8%) agreed that insulin should not be stopped after it was started.

Univariate analysis was used to analyse the association between demographic and clinical factors, and their willingness to accept insulin therapy (Table 3). Gender ($p=0.013$), knowing any relatives or friends have who used insulin ($p=0.004$) and doctor's recommendation ($p=0.019$) could significantly influence the patients' willingness to accept insulin. After adjusting for other demographic factors, multiple logistic regression showed that female patients were 1.67 times more likely to refuse insulin treatment if initiated (adjusted OR (AOR) 1.67, 95% CI 1.09-2.56, $p=0.018$). Patients who did not have any relatives or friends on insulin were 1.78 times more likely to refuse insulin if initiated (AOR 1.78, 95% CI 1.16-2.75, $p=0.008$). Patients who were never recommended insulin by their physician were 1.83 times more likely to refuse insulin if initiated (AOR 1.83, 95% CI 1.08-3.09, $p=0.024$).

In Table 4, univariate analysis demonstrated that all nine perception items showed significant associations with patients' willingness to accept insulin therapy. Multiple logistic regression showed that only restrictiveness, expected pain and low self-efficacy were significantly associated with insulin refusal. Patients who felt taking insulin would make their life less flexible (restrictiveness) were 2.43 times more likely to refuse insulin treatment (AOR 2.43, 95% CI 1.49-3.96, $p<0.001$). Patients who felt injecting insulin would be painful (expected pain) were 1.95 times more likely to refuse insulin (AOR 1.95, 95% CI 1.17-3.24, $p=0.010$). Patients who had lack of confidence in managing the demands of insulin therapy (low self-efficacy) were 1.79 times more likely to refuse insulin (AOR 1.79, 95% CI 1.11-2.90, $p=0.017$) (Table 4).

Table 1: Demographic and clinical characteristics of respondents (n=458)

Characteristics	Value
Age in years, mean \pm SD	56.7 \pm 10.9
Gender, n (%)	
Male	211 (46.1%)
Female	247 (53.9%)
Ethnicity, n (%)	
Malay	202 (44.1%)
Chinese	132 (28.8%)
Indian	124 (27.1%)
Education, n (%)	
No Formal Education	36 (7.9%)
Primary Education	167 (36.5%)
Secondary Education	214 (46.7%)
Tertiary Education	41 (9.0%)
Occupation, n (%)	
Government	44 (9.6%)
Private	108 (23.6%)
Self-employed	70 (15.3%)
Not Working	236 (51.5%)
Duration of diabetes, years, mean \pm SD	5.62 \pm 4.76
Fasting blood glucose level, mmol/L, mean \pm SD	7.94 \pm 2.81
HbA1C, %, mean \pm SD	7.75 \pm 1.63
Know that relatives / friends have ever used insulin, n (%)	
Yes	223 (48.7%)
No	235 (51.3%)
Taking Traditional & Complementary Medicine (T&CM) for DM treatment, n (%)	
Yes	63 (13.8%)
No	395 (86.2%)
Recommendation of insulin by doctor, n (%)	
Yes	78 (17.0%)
No	380 (83.0%)
Willingness to accept insulin if recommended by doctor, n (%)	
Yes	120 (26.2%)
No	338 (73.8%)

Table 2: Perceptions of diabetic patients towards insulin therapy (n=458)

Characteristics	n (%)	
	Agree	Disagree
Expected harm: Taking insulin can cause problems	80 (17.5%)	378 (82.5%)
Illness severity: Taking insulin means DM becomes much worse	196 (42.8%)	262 (57.2%)
Restrictiveness: Taking insulin would make life less flexible	302 (65.9%)	156 (34.1%)
Lack of fairness: Taking insulin would be just unfair	258 (56.3%)	200 (43.7%)
Expected pain: Injecting insulin would be painful	332 (72.5%)	126 (27.5%)
Risk of hypoglycaemia: Taking insulin would increase risk of hypoglycaemia	192 (41.9%)	266 (58.1%)
Low self-efficacy: Lack of confidence in managing the demands of insulin therapy	287 (62.7%)	171 (37.3%)
Personal failure: Taking insulin would means personal failure to manage disease	242 (52.8%)	216 (47.2%)
Permanence: Never quit insulin once it is started for DM treatment	283 (61.8%)	175 (38.2%)

Table 3: Association between patients' characteristics and willingness to accept insulin therapy

Variable	Willingness, n (%)		Crude OR	95% CI OR	χ^2 stat. (df) ^a	p-value ^a	AOR	95% CI OR	χ^2 stat. (df) ^a	p-value ^a
	Yes	No								
Age in years, mean ± SD	55 ± 10	57 ± 10	1.02	0.99;1.04	2.84 (1)	0.092				
Gender										
Male	67 (31.8)	144 (68.2)	1.00				1.00			
Female	53 (21.5)	194 (78.5)	1.70	1.12;2.60	6.23 (1)	0.013	1.67	1.09;2.56	5.89 (1)	0.018
Ethnicity					1.77 (2)	0.413				
Malay	56 (27.7)	146 (72.3)	1.00							
Chinese	29 (22.0)	103 (78.0)	1.36	0.81;2.28	1.39 (1) ^b	0.239 ^b				
Indian	35 (28.2)	89 (71.8)	0.98	0.59;1.61	0.01 (1) ^b	0.922 ^b				
Education					3.774 (3)	0.287				
No Formal Education	5 (13.9%)	31 (86.1%)	1.00							
Primary Education	48 (28.7%)	119 (71.3%)	0.40	0.15;1.09	3.21 (1) ^b	0.073 ^b				
Secondary Education	56 (26.2%)	158 (73.8%)	0.46	0.17;1.23	2.42 (1) ^b	0.120 ^b				
Tertiary Education	11 (26.8%)	30 (73.2%)	0.44	0.14;1.42	1.90 (1) ^b	0.169 ^b				
Occupation					7.732 (3)	0.052				
Government	9 (20.5%)	35 (79.5%)	1.00							
Private	38 (35.2%)	70 (64.8%)	0.47	0.21;1.09	3.10 (1)	0.078				
Self-employed	21 (30.0%)	49 (70.0%)	0.60	0.25;1.47	1.26 (1)	0.262				
Not Working	52 (22.0%)	184 (78.0%)	0.91	0.41;2.01	0.05 (1)	0.816				
Diagnosed as diabetic, years, mean ± SD	5.9 ± 5.31	5.5 ± 4.56	0.98	0.94;1.03	0.61 (1)	0.436				
Fasting blood glucose level, mmol/L, mean ± SD	8.3 ± 2.90	7.8 ± 2.76	0.94	0.87; 1.01	2.94 (1)	0.086				
HbA1C, %, mean ± SD	7.8 ± 1.85	7.7 ± 1.55	0.96	0.84, 1.08	0.52 (1)	0.472				
Know that relatives / friends have ever used insulin										
Yes	72 (32.3)	151 (67.7)	1.00				1.00			
No	48 (20.4)	187 (79.6)	1.86	1.22; 2.84	8.36 (1)	0.004	1.78	1.16; 2.75	6.41 (1)	0.008
T&CM for DM treatment										
Yes	15 (23.8)	48 (76.2)	1.00							
No	105 (26.6)	290 (73.4)	0.86	0.46; 1.61	0.22 (1)	0.639				
Recommendation of insulin by doctor										
Yes	29 (37.2)	49 (62.8)	1.00				1.00			
No	91 (23.9)	289 (76.1)	1.88	1.12;3.15	5.53 (1)	0.019	1.83	1.08;3.09	4.16 (1)	0.024

^a Likelihood Ratio (LR) test; ^b Wald test

Abbreviation: AOR – adjusted odds ratio; OR – odds ratio; SD – standard deviation; IQR – interquartile range; T&CM - Traditional & Complementary Medicine; DM – diabetes mellitus

Table 4: Association between patients' perceptions and willingness to accept insulin therapy

Variable	Willingness, n (%)		Crude OR	95% CI OR	χ^2 stat. (df) ^a	p-value ^a	AOR	95% CI OR	χ^2 stat. (df) ^a	p-value ^a
	Yes	No								
Expected harm: Taking insulin can cause problems										
Agree	13 (16.2)	67 (83.8)	2.04	1.08;3.84	5.38 (1)	0.020				
Disagree	107 (28.3)	271 (71.7)	1.00							
Illness severity: Taking insulin means DM becomes much worse										
Agree	33 (16.8)	163 (83.2)	2.46	1.56;3.87	16.08 (1)	<0.001				
Disagree	87 (33.2)	175 (66.8)	1.00							
Restrictiveness: Taking insulin would make life less flexible										
Agree	51 (16.9)	251 (83.1)	3.90	2.52;6.04	38.38 (1)	<0.001	2.43	1.49; 3.96	9.19 (1)	<0.001
Disagree	69 (44.2)	87 (55.8)	1.00				1.00			
Lack of fairness: Taking insulin would be just unfair										
Agree	49 (19.0)	209 (81.0)	2.35	1.54;3.59	15.81 (1)	<0.001	1.55	0.97; 2.47	2.43 (1)	0.064
Disagree	71 (35.5)	129 (64.5)	1.00				1.00			
Expected pain: Injecting insulin would be painful										
Agree	63 (19.0)	269 (81.0)	3.53	2.26; 5.51	30.69 (1)	<0.001	1.95	1.17; 3.24	5.80 (1)	0.010
Disagree	57 (45.2)	69 (54.8)	1.00				1.00			
Risk of hypoglycaemia: Taking insulin would increase risk of hypoglycaemia										
Agree	39 (20.3)	153 (79.7)	1.72	1.11; 2.66	6.04 (1)	0.014				
Disagree	81 (30.5)	185 (69.5)	1.00							
Low self-efficacy: Lack of confidence in managing the demands of insulin therapy										
Agree	52 (18.1)	235 (81.9)	2.98	1.94; 4.58	25.39 (1)	<0.001	1.79	1.11; 2.90	4.30 (1)	0.017
Disagree	68 (39.8)	103 (60.2)	1.00				1.00			
Personal failure: Taking insulin would mean personal failure to manage disease										
Agree	48 (19.8)	194 (80.2)	2.02	1.32; 3.09	10.78 (1)	0.001				
Disagree	72 (33.3)	144 (66.7)	1.00							
Permanence: Never quit insulin once it is start for DM treatment										
Agree	62 (21.9)	221 (78.1)	1.77	1.16; 2.70	6.95 (1)	0.008				
Disagree	58 (33.1)	117 (66.9)	1.00							

^a Likelihood Ratio (LR) test

Abbreviation: AOR – adjusted odds ratio; OR – odds ratio; SD – standard deviation

Discussion

Of 458 patients involved in this study, almost three quarter of the patients (73.8%) with T2DM seen in the public health clinics in South Seberang Perai District were not willing to accept insulin if initiated. This percentage was higher than several other studies done previously. As observed in other studies conducted by Zainuddin *et al.* 2011 in Kuala Lumpur, 50.7% of the respondents refused, Nadasen *et al.* 2012 in Durban, 56% of patients refused, Wong *et al.* 2011 at Singapore, 70.6% of the patients refused and Khan *et al.* 2008, conducted on Bangladeshi patients residing at East London with poorly controlled T2DM showed that 42.5% refused insulin therapy when it was initiated (8,12-14). Only in study done by Polonsky *et al.* 2005 United States of America showed a relatively low prevalence of insulin therapy refusal (i.e. 28.2%) (7). Compared to these studies, which were conducted in urban settings (where exposure of patients to healthcare services and health promotion are plenty) (8,12-14), the present study was conducted in the outskirts setting in Penang mainland where patient have limited access to health promotion and health information regarding their disease. This might explain why the patients were lacking proper understanding towards effective treatment options available for treating T2DM (8,15).

Hence, in this present study HbA1c level and duration of having T2DM did not significantly influence patients to accept insulin therapy. Previous study conducted by Tan *et al.* 2015 however, showed that HbA1c was a significant factor associated with insulin therapy refusal (9). This showed that patients were more concern on the route of taking medication than disease prognosis. In addition, female patients in this study with T2DM were more likely to refuse insulin therapy compared to their male counterpart, which coincides with the study conducted by Zainuddin *et al.* 2011 (8). Furthermore, most of the respondents were female (53.9%) and were not working (51.5%). This group of patients spent most of their time with family and close friends and may might easily accept any wrong information or myths that were passed on to them.

In addition, different with other studies that had been published beforehand, patients at South Seberang Perai District were more concerned on knowing either relatives or their close friends using insulin for them to accept insulin therapy. Mean age patients in this study was 56 years old, at this age patients most of the time will be with their family member or relatives. With proper support and encouragement for patients, they will be accepting insulin as a choice of therapy. These findings were highlighted in the study of Koin *et al.* 2010 in Japanese patients, which emphasizes the importance of family and friends support in improvement of clinical outcome of Diabetes Mellitus (16). As can be seen in this study, education level and occupation status did not contribute to influencing patient's initial decision of refusing insulin. In view of these, peer support group may be effective in promoting insulin acceptance among insulin naive diabetics as peer testimonies could facilitate insulin initiation.

In present study, it was also highlighted regarding the importance of physician recommendation of insulin during patient's clinical visit. Exposure to insulin treatment option during early phase of disease progression could produce more positive impact on patient's acceptance to receive insulin. A major setback in overcoming patient's negative misconception towards insulin is to curb emotional distress of patients living with diabetes for many years (6,7,17). Patient with T2DM will have high pill burden to manage the disease progression. Adding insulin will further complicate their life due to nature of insulin being an invasive procedure to apply. Therefore, it is important for clinicians and other healthcare providers to treat each patient with a more individualised approach – a treatment plan more custom made based on patient's routine and needs. It will be beneficial for patients to be exposed to the nature of diabetes, progression of disease which will lead to usage of insulin sooner or at a later part of the disease stage. Early education and focusing diabetic patient counselling by health care providers will clear patient's negative belief towards insulin.

There were three major barriers found in this study associated with unwillingness to initiate insulin therapy. Majority of the patients manifest several excuses for refusing insulin. Firstly, to the patients perception of taking insulin restrict their life and make it life less flexible. Due to current busy and active lifestyle, patient felt it is a big hassle to take along insulin with them everywhere. As highlighted in study by Hassan *et al.* 2013, patients were more worried whether the insulin therapy will hinder them from managing their work and personal commitments. Insulin injection requires special device to administer and must be kept at specific storage condition will further complicate patients' routine norm of life. Patients may feel uncomfortable and embarrassed taking insulin outside their home especially during travel (18). This led to more patients only opting for oral medication. Thus, it is important to *tailor-made* individualised insulin therapy plan based on patient daily routine can have a positive acceptance rate among T2DM patients.

Secondly, patients had negative perception on pain associated with insulin injection. Patient associate needle with pain thus they were reluctant to inject insulin. As highlighted in many previous studies,

fear of pain was one of major setback preventing patients from initiating insulin (7,8,12,17). Patient still have the perception of injecting insulin with needle and syringe. With the advancement of modern treatment newer devices are available which ease the administration process of insulin. Therefore, education and hands on demonstration to emphasize on the absence and negligence of pain during injecting insulin will change patients' negative perceptions of pain.

Thirdly, patients had low self-efficacy in handling insulin injection especially multiple injection regimen and frequently adjusted dosing based on their response. As shown in Polonsky et al. 2007, lack of self-efficacy was one of more pronounced negative attitudes in insulin refusal by patients (7). Similar observation was observed in Wong et al. 2011 and Tan et al. 2015 studies that patients fear of mishandling insulin device which might lead to treatment failure (9,13). A more comprehensive approach needs to be formulated to facilitate patient's understanding on insulin devices and injection method. More direct hands-on teaching method and more promotional material on ease of using insulin devices will help boost patient's confidence in handling it.

There were some limitations in this study, firstly this study included patients who had optimal diabetic control and suboptimal diabetic control. Patients in the first group might thought insulin therapy is not appropriate for them. Secondly, patient's compliance to the current treatment was not analysed in this study. Patients with poor compliance might feel that injecting insulin will just add burden to their current treatment. Lastly, in this study results were obtained from self-reported questionnaire by patients, it could not be ascertained whether patients' future response would be the same and the study was only conducted in the state of Penang and therefore the findings might not represent the whole population of Malaysia.

Conclusion

Current acceptance rate for insulin treatment is exceptionally low due to several negative perceptions of patients towards insulin with main rejection reasons were restrictiveness, expected pain and low self-efficacy. The data obtained from this study will help in facilitate to overcome patients reluctant to start insulin in clinical practice, especially with identified factors like gender, recommendation of insulin by doctor and knows relative or friends taking insulin have a significant influence on insulin acceptance. Educating patients to rectify the negative perception will improve overall acceptance rate, especially custom-made patient-centric approach will improve patient's initial negative perception towards insulin therapy.

Acknowledgements

We thank the Director General of Health, Malaysia for his permission to publish this paper. We also would like to express our very great appreciation to all the staff involved in assisting our study. Our special thanks are extended to all the participants in this study.

Conflict of Interest Statement

This study was not funded by any organisation and has no conflict of interest.

References

1. World Health Organisations. Diabetes mellitus. [updated 2017; cited 2017 May 12]. Available from <http://www.who.int/mediacentre/factsheets/fs138/en/>
2. Diabetes Malaysia. What is diabetes. [updated 2006 Dec 28; cited 2017 May 12]. Available from <http://www.diabetes.org.my/article.php?aid=5>
3. Ministry of Health Malaysia. National health & morbidity survey 2015 non-communicable diseases, risk factors & other health problems volume II. Malaysia: Institute for Public Health 2015. 14.
4. Ellis, Kathy & Mulnier, Henrietta & Angus, Forbes. (2018). Perceptions of insulin use in type 2 diabetes in primary care: A thematic synthesis. *BMC Family Practice*. 19. 10.1186/s12875-018-0753-2. 4
5. Peyrot M, Rubin RR, Lauritzen T, Skovlund SE, Snoek FJ, Matthews DR, Landgraf R, Kleinbreil L; International DAWN Advisory Panel. Resistance to insulin therapy among patients and providers: results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. *Diabetes Care*. 2005 Nov;28(11):2673-9. doi: 10.2337/diacare.28.11.2673. PMID: 16249538. 5
6. Polonsky WH, Fisher L, Guzman S, Villa-Caballero L, Edelman SV. Psychological insulin resistance in patients with type 2 diabetes. *Diabetes Care*. 2005 Oct 1;28(10):2543-5. 6
7. Polonsky W. Psychological Insulin Resistance. *The Diabetes Educator*. 2007 Jul;33(7s):241S-4S. 7
8. Zainuddin NA, Zulkarnain AK, Tahir A. Psychological insulin resistance (PIR) among type 2 diabetes patients at public health clinics in federal territory of Malaysia. *The International Medical Journal of Malaysia*. 2011;10(2). 8

9. Tan WL, Asahar SF, Harun NL. Insulin therapy refusal among type II diabetes mellitus patients in Kubang Pasu district, Kedah, Malaysia. *Singapore Medical Journal*. 2015; 56(4); 224-227 9
10. Saleem A, Masood I, Khan TM. Insulin perception among insulin-naïve type-2 diabetes mellitus patients in Pakistan. *Cogent Medicine*. 2016 Dec 31;3(1):1229374. 10
11. Israel GD. Determining sample size. Gainesville: University of Florida Cooperative Extension Service, Institute of Food and Agriculture Sciences, EDIS; 1992 Nov. 11
12. Nadasen DM, Naidoo M. Patients with type 2 diabetes and difficulties associated with initiation of insulin therapy in a public health clinic in Durban: original research. *South African Family Practice*. 2012 Sep 1;54(5):436-40. 12
13. Wong S, Lee J, Ko Y, et al. Perception of insulin therapy amongst Asian patients with diabetes in Singapore. *Diabet Med* 2011; 28:206-11 13
14. Khan, Hussein & Lasker, S & Chowdhury, Tahseen. (2008). Prevalence and reasons for insulin refusal in Bangladeshi patients with poorly controlled Type 2 diabetes in East London. *Diabetic medicine : a journal of the British Diabetic Association*. 25. 1108-11. 10.1111/j.1464-5491.2008.02538.x. 14
15. Khoo EM, Lee YK, Ng CJ, Lee PY, Abdullah KL, Low WY, Abdul Samad A, Chen WS. What are the barriers faced by patients using insulin? A qualitative study of Malaysian health care professionals' views. *Patient preference and adherence*. 2013;3(7):103-9. 15
16. Watanabe K, Kurose T, Kitatani N, Yabe D, Hishizawa M, Hyo T, Seino Y. The role of family nutritional support in Japanese patients with type 2 diabetes mellitus. *Internal Medicine*. 2010; 49; 983-989 16
17. Polonsky WH, Hajos TRS, Dain MP, Snoek FJ. Are patients with type 2 diabetes reluctant to start insulin therapy? An examination of the scope and underpinnings of psychological insulin resistance in a large, international population. *Current Medical Research & Opinion*. 2011; 27(6); 1169-1174 17
18. Hassan HA, Tohid H, Amin RM, Bidin MB, Muthupalaniappen L, Omar K. Factors influencing insulin acceptance among type 2 diabetes mellitus patients in a primary care clinic: a qualitative exploration. *BMC family practice*. 2013 Oct 29;14(1):164. 18

Medication Errors Understanding among the Healthcare Providers at the Health Clinics in Labuan Federal Territory

Mohd Arrif Md Zahary¹, Eddie Ha Hsiao Lung¹, Farah Ayuni Ghazali¹, Caroline Esther Paul¹

¹ Labuan Federal Territory Health Clinic, Federal Territory Labuan, Ministry of Health Malaysia

Abstract

Introduction: As an early step to prevent medication error, strengthening the healthcare providers' knowledge about medication error is needed.

Objectives: This study aimed to assess the healthcare providers' knowledge and perception towards medication error and medication error reporting at the health clinics in Labuan Federal Territory.

Methods: This was a cross-sectional survey in which self-administered questionnaires were given to all healthcare providers except pharmacy's staffs working at the government health clinics in Labuan from 30 July 2018 to 17 August 2018. The questionnaire consisted of 4 parts, including demographic data, knowledge on medication error, perception towards medication error and perception towards medication error reporting.

Results: A total of 132 respondents were involved in the study. Only about 35% (n=46) of respondents answered all the questions about knowledge on medication error correctly. In terms of perception towards medication error, 95.4% (n=126) of the respondents thought that medication error is avoidable, and 87.8% (n=116) disagreed that it is not necessary to report if a medication error occurs but does not harm the patient. In terms of perception towards medication error reporting, 40.2% (n=53) of respondents were afraid of the negative consequences associated with medication error reporting.

Conclusion: The knowledge level of healthcare providers on medication error were still low despite generally positive perceptions towards medication error reporting. The knowledge on medication error needs to be improved through continuous education in order to increase medication error reporting and reduce medication errors.

Keywords: medication error, healthcare providers, look-alike sound-alike, knowledge

NMRR ID: NMRR-17-2411-38085

Corresponding Author: Caroline Esther Paul

Pharmacy Unit, Labuan Federal Territory Health Clinic, P.O. Box 81736, 87027 Labuan Federal Territory.

Email: carolineesther@moh.gov.my

Introduction

Medication error is any preventable event that leads to inappropriate use of medication and patient harm while the medication is under the healthcare providers' control (1,2). Among the common types of medication errors are prescribing errors, wrong dose errors and wrong drug errors. Medication error can cause harms to the patient such as severe injury or death (1). A study had shown that the prevalence of medication errors was 30.5% at an emergency department of a hospital in Malaysia (3). Other studies have also shown that medication errors are common issues occurring in the healthcare facilities and there were a few contributing factors identified, including individual, organization and working environment. Medication error may be committed by both experienced and inexperienced healthcare provider (4).

Patient safety is a common goal for every healthcare provider. Medication error reporting is a way of addressing the event of a medication error and the reporting is very important so that all healthcare providers can learn from it and thus improving the awareness regarding medication safety. Health managers generally considered preventing medication error as a high priority and healthcare providers need to take action towards medication error reports. Staffs are encouraged to report medication error and understand the negative consequences associated with medical error to reduce medical error incidents (5). The Pharmaceutical Services Programme of Ministry of Health Malaysia established the Medication Error Reporting System (MERS) since 2009. It is a national reporting system that serves as a platform to encourage healthcare professionals to report any medication error encountered (1).

A study reported that healthcare providers could have different levels of awareness on medication error and poor knowledge on medication error may affect the reporting of medication errors (6). Thus, knowing the medical staffs' understanding level about medication error is required to strengthen the current system of medication error reporting and prevent medication error. The aim of this study was to assess Labuan Federal Territory government health clinics' healthcare providers' knowledge and perception towards medication error. The finding from this study could help to strategise the plan to improve the perspective of healthcare providers towards the reporting of medication errors.

Methods

The study was a cross-sectional survey with self-administered questionnaires from 30 July 2018 to 17 August 2018. The study population involved all healthcare providers working at the health clinics in Labuan Federal Territory.

The questionnaire was developed, adapted and modified from literature review, in both English and Malay language. The validation of the questionnaire was done within the facility. The questionnaire consisted of four parts, which include demographic data, knowledge on medication error, perception towards medication error and perception towards medication error reporting. Part A (demographic data) had four questions. Part B had six questions that test the knowledge of healthcare providers on the facts about medication error, look alike sound alike (LASA) medications and Tallman lettering. A respondent was considered as having good knowledge if all the six questions were answered correctly. Part C consisted of six questions that assess the perceptions of healthcare providers towards medication errors. Part D had six questions to assess the perceptions of healthcare providers towards medication error reporting and three questions about the experience of medication error reporting. The answers to the perception questions in Part C and Part D were in the form of three-point Likert scale with the choices of disagree, neutral and agree.

The questionnaires were distributed to all healthcare providers working in the Labuan Federal Territory health clinics and were collected after three weeks. Permanent healthcare providers, including medical officers, medical assistants, nurses and dentists, working in the Outpatient Services, Maternal dan Child Health Clinic, ten Rural Clinics, Taman Mutiara Community Clinic, Dental Clinics and Urban Transformation Centre (UTC) Health Clinic were included in the study. The pharmacists and pharmacist assistants working in the health clinics were excluded because the study was conducted by the pharmacy unit. Participation in this research was entirely voluntary.

Data analysis was done using Microsoft Excel Worksheet. The frequency and percentage of responses were counted and tabulated according to knowledge on medication error, perceptions towards medication error and perceptions towards medication error reporting.

Results

A total of 165 questionnaires were distributed and the response rate was 80%. Thirty-three questionnaires were not returned. Among the 132 respondents, the majority of respondent were female (87.1%), aged 26-35 years old (58.3%) and with more than 10 years working experience (38.6%). Only a minority of the respondents had good knowledge on medication error (34.8%). Overall, the Medical Officers had the best understanding towards medication error, with 62.9% of them being able to obtain all correct answers (Table 1).

In terms of perception towards medication error (Table 2), 95.4% of the respondents agreed that medication errors were avoidable, and majority agreed that tiredness or stress level of healthcare providers (93.9%), not following the standard operating procedures (80.3%) and heavy workload (87.1%) contributed to medication errors. Most of them disagreed that it is not necessary to report a medication error that does not harm the patient (87.8%), and medication error is an embarrassing topic to discuss with colleagues (77.3%).

In terms of perceptions towards medication error reporting (Table 3), there were mixed opinions about the liability for legal punishment and fear of negative consequences associated with medication error reporting. A high proportion of respondents disagreed that reporting medication error is not important (88.6%) and agreed that the staffs were supported for reporting medication error in their workplace (91.7%). Most respondents agreed that their departments take corrective actions based on the reported medication errors to improve medication safety (94.7%), and medication error reporting prevents the similar medication error from reoccurring (96.7%). Despite the positive perceptions towards medication error reporting, only 14 respondents (10.6%) declared that they had ever reported a medication error (Table 4).

Table 1: Demographic data of healthcare providers included in the study and their knowledge level about medication error (n=132)

	Healthcare Providers, n (%)				Total
	Medical Assistant	Medical Officer	Dentist	Nurse	
Gender					
Male	9 (90.0)	6 (22.2)	1 (6.7)	1 (1.3)	17 (12.9)
Female	1 (10.0)	21 (77.7)	14 (93.3)	79 (98.8)	115 (87.1)
Age group					
Below 25 years	4 (40.0)	0	9 (60.0)	0	13 (9.8)
26 – 35 years	6 (60.0)	25 (92.6)	5 (33.3)	41 (51.2)	77 (58.3)
36 - 45 years	0	2 (7.4)	0	29 (36.3)	31 (23.4)
Above 45 years	0	0	1 (6.7)	10 (12.5)	11 (8.3)
Working experience					
Below 1 year	0	0	7 (46.4)	0	7 (5.3)
1 – 5 years	9 (90.0)	20 (74.1)	7 (46.4)	13 (16.3)	49 (37.1)
6 - 10 years	1 (10.0)	6 (22.2)	0	18 (22.5)	25 (18.9)
Above 10 years	0	1 (3.7)	1 (6.7)	49 (61.3)	51 (38.6)
Knowledge					
Good	3 (30.0)	17 (62.9)	2 (13.3)	24 (30.0)	46 (34.8)
Inadequate	7 (70.0)	10 (37.1)	13 (86.7)	56 (70.0)	86 (65.2)

Table 2: Perceptions of healthcare providers towards medication error (n=132)

Question	Disagree, n (%)	Neutral, n (%)	Agree, n (%)
1. Tiredness or stress of staff may cause medication errors.	7 (5.3)	1 (0.8)	124 (93.9)
2. A medication error is avoidable.	2 (1.5)	4 (3.0)	126 (95.4)
3. A medication error is a result of standard operating procedures that were not followed.	8 (6.1)	18 (13.6)	106 (80.3)
4. It is not necessary to report if a medication error occurs but does not harm the patient.	116 (87.8)	8 (6.0)	8 (6.0)
5. It is embarrassing to discuss medication error with colleagues.	102 (77.3)	19 (14.4)	11 (8.3)
6. A heavy workload will increase the number of medication errors.	7 (5.33)	10 (7.6)	115 (87.1)

Table 3: Perceptions of healthcare providers towards medication error reporting (n=132)

Question	Disagree, n (%)	Neutral, n (%)	Agree, n (%)
1. Persons responsible for medication error are liable for legal punishment.	59 (44.7)	45 (34.1)	28 (21.2)
2. I am afraid of the negative consequences associated with medication error reporting.	41 (31.3)	38 (28.8)	53 (40.2)
3. It is not important to report a medication error.	117 (88.6)	8 (6.1)	7 (5.3)
4. Staffs are supported for reporting medication error in my workplace.	5 (3.8)	6 (4.5)	121 (91.7)
5. My department takes corrective action on reported medication error (near-miss/ incident) to improve medication safety.	0	7 (5.3)	125 (94.7)
6. Reporting of the medication error prevents the same medication error from reoccurring.	1 (0.8)	3 (2.3)	128 (96.7)

Table 4: Proportion of the action taken by the healthcare providers to report the medication error (n=14)

HCP	HCP that had ever reported ME, n (%)	ME reporting method, n (%)		
		MERS online	ME manual form	Report to superior
Medical assistant	3 (2.3)	0	0	3 (21.4)
Medical officer	3 (2.3)	0	1 (7.1)	2 (14.3)
Dentist	1 (0.8)	0	0	1 (7.1)
Nurse	7 (5.3)	1 (7.1)	0	6 (42.9)
Total	14 (10.6)	1 (7.1)	1 (7.1)	12 (85.7)

Abbreviation: HCP – healthcare provider; MERS – medication error reporting system; ME – medication error

Discussion

As defined by the United States National Coordinating Council for Medication Error Reporting and Prevention, medication error is “any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures and systems, including prescribing, order communication, product labelling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use” (2). This study revealed that medication error knowledge was still unsatisfactory, with only about 35% among the healthcare providers working in the health clinics in Labuan Federal Territory. A poor understanding about medication error among the practicing healthcare providers could result in significant risk for medication error (7).

Among the questions in the Knowledge domain of the questionnaire were questions about the need to store LASA medications separately and using Tallman lettering to prevent medication error. According to World Health Organisation (WHO), the existence of confusing drug names is one of the most common causes of medication error and is of concern worldwide (8). The Institute for Safe Medication Practices (ISMP) published the list of medication name pairs commonly involved in medication error and many LASA combinations could potentially cause error (9). LASA medications with spelling similarities or similar phonetics and even product packaging may at some point contribute to medication error (10). Therefore, education and promotion on the management of LASA medications are needed as there were still under-exposure among the healthcare providers as shown in this study. One of the preventions of medication errors related to LASA medications is by separating them from their pair. As simple as just storing the LASA medications separately and avoiding immediate proximity to one another will create a safer environment for medication safety (9,10). In addition, the Ministry of Health Malaysia promotes the practice of Tall Man lettering to differentiate the sound-alike medications' names, by means of writing part of medicine name in upper case letters to provide distinction between LASA from one another. This is especially crucial for medications in the emergency trolleys (10).

From our findings, the majority of healthcare providers agreed that staff wellbeing (tiredness or stress level), failure to comply to standard operating procedures, and a heavy workload might contribute to medication errors. Another study also supported that heavy workload was one of the highest contributing factors contributing to medication errors among the nurses in government hospitals (11). Heavy workload may cause staff tiredness and affect their stress level, which may eventually increase the number of medication errors. All these three factors were preventable and must be taken care of to ensure patient safety and to provide a high-quality healthcare services to the public.

One of the ways to create awareness for medication safety is by reporting medication errors. However, under-reporting of medication error is an issue, and this could be due to several factors that hindered the healthcare providers from reporting medication errors. Our study demonstrated that the majority of healthcare providers agreed that it was important to report medications error (88.6%), but almost half (40.2%) of them were afraid of the negative consequences associated with medication error reporting. Therefore, emotion and beliefs about the consequences could be the major barriers that hindered medication error reporting among healthcare providers at health clinics in Labuan Federal Territory. Stewart *et al.* (2018) discussed the facilitators and barriers to medication error reporting among healthcare providers in Qatar, among which the emotions (fear and worry) and beliefs about the consequences were the major barriers to medication error reporting, particularly among the younger and less experienced healthcare

providers (12). Healthcare providers could be afraid to report medication error, which may affect their performance evaluation and career progression. In addition, the impact on working relationships among the colleagues and the potential lack of confidentiality were also among the few negative perceptions on medication error reporting.

In this, only 10.6% of healthcare providers had ever reported a medication error. The issue of medication error under-reporting was addressed in many studies which believed there could be a high number of medication error cases, but the cases were limitedly reported (13-15). A hospital in Ireland demonstrated that medication error reporting level was increased substantially when a system of regular feedback to staff was introduced to encourage continuing reporting and improve the awareness for medication safety. The hospital implemented a medication safety project that involved the appointment of a medication safety facilitator, establishing an online reporting system, and eliminated the focus on personal failure. All the reported events were responded with devised action plans and alerts, and separate bulletins for nursing and medical staff were also made to highlight the risk reduction measures relevant to their practice scopes (16).

The main limitation of the study was the three-week period between the distribution of questionnaires and collection of responses. Furthermore, the respondents answered the questionnaires without being monitored by the investigators and discussion among the respondents were possible and thus, may affect the findings of the study.

Conclusion

Medication errors understanding among the healthcare providers working at the government health clinics in Labuan Federal Territory was unsatisfactory. However, majority of healthcare providers have good perception towards medication error and its reporting. In order to increase medication error reporting, continuous education and training of standard operational procedure of medication error reporting need to be provided regularly by the pharmacists to other healthcare providers.

Acknowledgement

The authors would like to thank the Director General of Health for permission to publish this paper. Special thanks to all the individuals who have contributed to this study.

Conflict of Interest Statement

No external funding was received and the authors declared no conflict of interest.

References

1. Guideline on Medication Error Reporting, 1st ed., Ministry of Health Malaysia, 2009.
2. National Coordinating Council for Medication Error Reporting and Prevention. What is a medication error? New York, NY: National Coordinating Council for Medication Error Reporting and Prevention; 2015. Available from: <http://www.nccmerp.org/about-medication-errors> (accessed 12 December 2018).
3. Shitu et al., Prevalence and Characteristics of Medication Errors at An Emergency Department of a Teaching Hospital in Malaysia. *BMC Health Service Research*, 2020.
4. Denham et al., Medication Safety in Community Pharmacy: A Qualitative Study of the Sociotechnical Context. *BMC Health Service Research*, 2009.
5. Teoh et al., Perceptions of Doctors and Pharmacists Towards Medication Error Reporting and Prevention in Kedah, Malaysia: A Rasch Model Analysis. *Advances in Pharmacoepidemiology and Drug Safety*, 2015;4(5).
6. Abdel-Latif M.M. et al., Knowledge of healthcare professionals about medication errors in hospitals. *J Basic Clin Pharma*, 2016; 7:87-92.
7. Simonsen BO, Johansson I, Daehlin GK, Osvik LM, Farup PG. Medication knowledge, certainty, and risk of errors in health care: a cross-sectional study. *BMC Health Serv Res.*, 2011; 11:175. doi: 10.1186/1472-6963-11-175.
8. World Health Organization (WHO): Look-Alike, Sound-Alike Medication Names. Available from: <http://www.who.int/patientsafety/solutions/patientsafety/PS-Solution1.pdf>
9. Institute for Safe Medication Practices (ISMP): List of confused drug names. Huntingdon Valley, PA, Institute for Safe Medication Practices. 2015. Available from: <http://www.ismp.org/Tools/confuseddrugnames.pdf>
10. Guide on Handling Look-Alike, Sound-Alike Medications 1st ed. Ministry of Health Malaysia, 2012.
11. Johari, H., Shamsuddin, F., Idris, N., & Hussin, A., Medication Errors Among Nurses in Government Hospital. *IOSR Journal of Nursing and Health Science (IOSR-JNHS)*, 2013, 18-23.

12. Stewart et al., Exploring Facilitators and Barriers to Medication Error Reporting among Healthcare Professionals in Qatar Using Theoretical Domains Framework. A mixed-method approach 2018; 14-17.
13. Mrayyan, M. T., Shishani, K. and Al-Fouri, I., Rate, causes and reporting of medication errors in Jordan: nurses' perspectives. *Journal of Nursing Management*, 2017, 15: 659-670.
14. Bayazidi, S., Zarezadeh, Y., Zamanzadeh, V., & Parvan, K., Medication Error Reporting Rate and its Barriers and Facilitators among Nurses. *Journal of caring sciences*, 2012, 1(4), 231-6.
15. Ross LM, Wallace J, Paton JY Medication errors in a pediatric teaching hospital in the UK: five years of operational experience. *Archives of Disease in Childhood*, 2000; 83:492-497.
16. Eileen et al., Medication Safety in an Acute Teaching Hospital: an Irish Prospective. *Italian Journal of Public Health*, 2005.

eISSN 2637-1332



9 772637 133000