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EMERGENCY DEPARTMENT VISIT DUE TO MEDICATION NON-ADHERENCE AT A TEACHING HOSPITAL IN MALAYSIA

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ABSTRACT: Background: Medication non-adherence is a growing burden to the health care system in Malaysia. **Aim:** The study aimed to determine the prevalence, severity, outcome, and factors associated with emergency department (ED) visit due to medication non-adherence at a teaching hospital in Malaysia. **Methods:** A cross-sectional study design was conducted on patients at the ED of Hospital Universiti Sains Malaysia over six weeks from December 2014 to January 2015. Data were collected using patient interview and review of patient's medical records. Statistical analysis: Descriptive statistics and multiple logistic regression. **Results:** Out of the 434 patients on ED visit, 63 (14.5%) [95%CI, 11.0%, 18.0%] were related to medication non-adherence, out of which, 53 (84.1%) experienced severe outcome of the ED visit, 48 (76.2%) were admitted to the ED observation ward, 10 (15.9%) to the hospital ward and 5 (7.9%) were discharged immediately after they have consulted with the ED-physician. Factors associated with the ED visit due to medication non-adherence were: cardiovascular disorder [OR: 7.5 (95%CI 5.3, 11.0)], tuberculosis [OR: 5.5 (95% CI 2.8, 10.6)], asthma [OR: 2.6 (95% CI, 1.7, 4.4)], diabetes mellitus (type II) [OR: 0.2 (95%CI, 0.1, 0.4)], central nervous system disorder [OR: 3.8 (95% CI, 2.2, 5.6)] and consulting multiple prescribers [OR: 0.4 (95%CI, 0.2, 0.8)]. **Conclusion:** Medication non-adherence is a significant contributor to ED visit, especially among patients with chronic illnesses in Malaysia. More intervention measures should be focused on people with chronic diseases.

Keywords: Medication non-adherence, adverse drug event, Emergency Department, Malaysia

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INTRODUCTION: An adverse drug event (ADE) is defined as "any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment" [1].

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Medication non-adherence is one of the major causes of ADE associated with therapeutic drug failure. It has been a significant contributor to economic and healthcare-burden [2, 3]. In the United States, it has been described as a "hidden healthcare problem" and "America's other drug problem(s)" [3, 4].

Medication non-adherence has been associated with drug-related morbidity and mortality arising from drug treatment failure, sub-optimal management of illness, increased risk of chronic complications, and emergency department (ED)

visit [5, 6]. This problem was responsible for over 12,000 deaths annually, 30 to 60% of drug-related hospital admission and 2% to 25% of ED visits [7-10]. In terms of health care cost, medication non-adherence has also contributed to over $100 increase in healthcare expenditure [11].

Medication non-adherence was found predominantly among patients with chronic disorders such as hypertension, diabetes, tuberculosis, asthma, and human immuno-deficiency virus (HIV) [12, 13]. According to WHO, adherence to long term therapies was about 50% in developed countries and expected to be lower than that in developing countries.[8] Malaysia has a high prevalence rate of diabetes mellitus (DM), hypertension, tuberculosis (TB), and asthma,[14] however, the few studies on medication non-adherence reported medication non-adherence rate of 40 to 70% in patients with DM, TB, hypertension, and schizophrenia in Malaysia [6,15-17].

Previous studies on drug-related hospital admission in Malaysia has shown medication non-adherence as a leading cause of therapeutic failure leading to hospitalization [18]. To our knowledge, there have been no data on the emergency department visit related to medication non-adherence in an ED setting in this country.

We previously reported a 30.6% prevalence rate of drug-related visits to the emergency department in a teaching hospital in Malaysia [19]. In the present study, we further investigated the prevalence, severity, outcome, and factors associated with the visits.

MATERIALS AND METHODS: Cross-Sectional study design was conducted on ED patients at an ED of Hospital Universiti Sains Malaysia, over six weeks in December 2014 and January 2015. The study protocol was approved by the institutional ethics committee and included patients or patient caretaker in case of a child of seriously ill was asked to complete a consent form before the study. The inclusion criteria included patients on ED visit 09:00 am to 05:00 pm (Sunday to Thursday) during the study period. The exclusion criteria included patients on referral from other hospitals, scheduled visits, and medico-legal cases. The ED visit was considered to be due to medication non-adherence when the chief presenting complaint at the ED was associated with the inability of the patient to adhere with the treatment schedules within 48 h or more as recommended by a physician [20, 21]. The details of the study protocol and the data collected have been described and previously published [19].

Data Analysis: The data were analyzed using statistical software (SPSS version 21, SPSS Inc, Chicago, Illinois). The prevalence of ED visit due to medication non-adherence was calculated by dividing the number of patients with ED visit due to medication non-adherence by the total number of sample size (434). The results of the descriptive analysis were presented as frequency (percentages) for categorical variables and mean (standard deviation) (SD) for numerical variables. Chi-square goodness-of-fit test was used to determine statistical differences of cases in a single categorical variable. In the determination of factors associated with ED visit due to medication non-adherence, simple logistic regression was used in the univariable analysis to screen variables for multiple logistics regression.

The multiple logistic regression was performed using forward logistic regression. Multicollinearity and interaction were all checked, model fitness was assessed using the Hosmer-Lemeshow test, classification table, and area under the (ROC) curve. The independent predictors of ED visit due to medication non-adherence were determined at the final model. Results were expressed as adjusted odds ratio (OR) with 95% CI.

RESULTS: There were 7,530 total ED visits over the six weeks. A detail of the results for the patient selection has been previously published. Out of the 434 eligible patients interviewed, sixty-three patients had an ED visit related to medication non-adherence. A prevalence rate of ED visit due to medication non-adherence was determined as [(14.5%) 95% CI 11.0, 18.0%]. **Table 1** demonstrates the characteristics of the patients.

The classes of drugs most commonly involved were antihypertensive (39.7%), oral hypoglycaemic drugs (22.2%), insulin (9.5%), anticonvulsant (7.9%), anti-asthmatic (6.3%) and antipsychotics (4.8%). The reasons for the non-adherence were; inadequate medication monitoring in the elderly

(23.6%), switching over to complementary and alternative medicine (CAM) use (20.6%), mental illness (15.9%), Inconvenient route of drug administration (14.3%), busy lifestyle (11.1%) and adverse drug reactions (9.5%). Fifty-three (84.1%) and 10 (15.9%) of the patients suffered the severe and mild outcome of the ED visits, respectively. The most dominant complaints were hypertensive urgency, hyperglycemia, seizure, abnormal behavior and shortness of breath. There was no death or permanent disability reported. Forty-eight (76.2%) patients were admitted to the ED observation ward for a maximum of 72 h, 10 (15.9%) were discharged immediately after they have consulted with the ED-physician, and 5 (7.9%) were admitted to the hospital ward.

TABLE 1: CHARACTERISTIC OF 63 PATIENTS WITH ED VISIT DUE TO MEDICATION NON-ADHERENCE

Variables	Mean (SD)[1]	Frequency n (%)	P value[2]
Gender			
Male		25 (39.7)	0.101
Female		38 (60.3)	
Age	52.4 (16.03)		
≤9		1 (1.6)	<0.001
10-19		0 (0.0)	
20-29		6 (9.5)	
30-39		7 (11.1)	
40-49		6 (9.5)	
50-59		20 (31.7)	
≥60		23 (36.5)	
Marital status			
Single		18 (28.6)	<0.001*
Married		44 (38.5)	
Divorcee		1 (1.6)	
Ethnicity			
Malay		61(96.8)	<0.001*
Chinese		2 (3.2)	
Education			
No formal education		29 (46.0)	0.529
Formal Education		34 (54.0)	
Employment			
Unemployed		59 (93.3)	<0.001
Employed		4 (6.3)	
Current CAM use[3]			
No		54 (85.7)	<0.001
Yes		9 (14.3)	
Consulting multiple prescribers			
No		40 (63.5)	0.032
Yes		23 (36.5)	
Presence of co-morbidity			
No		23 (36.5)	0.032
Yes		40 (63.5)	
History of drug Allergy			
No		58 (92.1)	<0.001
Yes		5 (7.9)	
Presence of chronic diseases			
Cardiovascular system disorder		28 (44.4)	<0.001
Diabetes mellitus (type II)		20 (31.8)	
Central nervous system disorder		8 (12.7)	
Asthma		4 (6.4)	
Tuberculosis		3 (4.8)	

Factors associated with ED visit due to medication non-adherence: Table 2, shows the results of multiple logistic regression of factors associated with ED visits due to medication non-adherence.

TABLE 2: FACTORS ASSOCIATED WITH ED VISIT DUE TO MEDICATION NON-ADHERENCE

Variables	Adjusted odds ratio[1] (95% CI)	P-value
Consulting multiple prescribers[2]	0.4 (0.2, 0.8)	0.010
Presence of chronic diseases:		
Diabetes mellitus	0.2 (0.1, 0.4)	<0.001
Central nervous system disorders	3.83 (2.2, 5.6)	<0.001
Cardiovascular disorder	7.5 (5.3, 11.00)	<0.001
Asthma	2.55 (1.7, 4.4)	0.004
Tuberculosis	5.6 (2.8, 10.6)	0.008

[a]Forward Logistic Regression model was applied
Multicollinearity and Interaction term were checked and were not found
Hosmer-Lemeshow test (p=0.975) and classification table (overall correctly classified percentage=86.9%) and area under the ROC curve= 88.1% were applied to check the model fitness and reported to be fit.
[*]Consulting multiple prescribers in the last two weeks before the ED visit

DISCUSSION: To our knowledge, the current study was the first to report the prevalence rate of ED visit due to medication non-adherence at a teaching hospital in Malaysia. The prevalence rate in the current study was consistent with other studies (7.6% to 25.5%) [9, 22], and higher than two retrospective studies conducted in United States and Saudi-Arabia (0.13 and 2.0%) respectively [3, 23], However, retrospective studies have been identified with underestimation of ADE-related ED visit[5]. Moreover, the high prevalence rate may be attributed to a higher proportion of patients with chronic diseases in our study, which were earlier associated with non-adherence to medication [3,12, 13].

A high proportion of ED visits due to medication non-adherence was observed among the elderly (≥60 years) patients. The elderly patients were also found to have a high prevalence rate of chronic diseases, thus, predisposing them to multiple medication use for a longer period and increase the likelihood of medication non-adherence. More than 80% of the patients with ED visit due to medication non-adherence in the current study experienced the severe outcome of the ED visit.

This could be because, in the current study, the majority of the patients were presented with hypertensive urgencies and hyperglycemia related to non-adherence to antihypertensive and antidiabetics.

More than half of the patients were admitted to the ED observation ward. This indicated the need for the services of a clinical pharmacist in the ED, for adequate detection of ADE and patient counseling. About 10% of the patients were admitted to hospital ward through the ED; this is lower than a study on drug-related hospital admission in Malaysia that reported a proportion of 40% of hospital admissions due to medication non-adherence [16]. The reason may be because, most the patients with medication non-adherence were admitted to the ED observation ward to a maximum period of 72 hours, as such, high number of them were discharged from the ED without admitting them to the hospital ward.

In the current study, patient with underlying chronic illnesses and those that visited multiple prescribers in the last 14 days before the ED were found to have high chances of ED visit due to medication non-adherence. This is similar to other studies [9, 20]. The reason may be related to the high proportion of patients with chronic illnesses reported in the study, which is also a reflection of the current prevalence rate of chronic diseases in Malaysia [19, 24].

Inadequate medication monitoring in the elderly with chronic illness was the most reported reason for defaulting to medication schedules in the current study. The reason may be related to a high population of elderly people (≥ 60 years) in Malaysia, with the majority of them having one or more chronic illness [24, 25]. Another report showed that most of this elderly lack adequate care at home, often left alone without medication monitoring [26]. Moreover, there is also inadequate geriatric care services such as nursing homes, drop-ins, home-care, geriatric clinics, and family medicine specialist in Malaysia to cater to the increasing number of the elderly population [26]. Full implementation of national policies such as the National Social Welfare Policy (1990), National Policy for the Elderly (1990), and National Council of the Senior Citizen's Organisation of Malaysia

(NCSCOM), targeted at the elderly, is, therefore, necessary to provide adequate care for the elderly [27]. In Malaysia, interventions such as the implementation of Medication Therapy Adherence Clinics (MTAC) services for some chronic diseases and run by pharmacists in selected public hospitals has resulted in significant improvements in medication adherence [28]. Further intervention measures such as the implementation of geriatric-ED guidelines, quality indicators for geriatric care, and the establishment of more MTAC clinics in all hospitals [29].

CONCLUSION: Medication non-adherence is a significant contributor to ED visit, especially among the elderly with underlying chronic diseases in Malaysia.

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CONFLICT OF INTEREST: All authors declare no conflict of interest

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