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CONTENTS

A Study on Medication Nonadherence Among Geriatric Patients with Diabetes Mellitus at Health Clinics in Marang District, Terengganu

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Abstract

Introduction: Type-2 Diabetes Mellitus (T2DM) was considered a global health condition that affected millions of geriatric populations with an increasing prevalence. Despite the clear advantages of medication adherence towards lowering the risks of mortality and vascular complications, the issues of medication nonadherence remained unsettled.

Objective: This study aimed to assess the rate of medication nonadherence and identify the factors associated with medication nonadherence among geriatric patients with diabetes mellitus in the health clinics of Marang District.

Methods: This cross-sectional study was conducted in six public health clinics in Marang district, Terengganu, involving geriatric patients diagnosed with diabetes mellitus. Data was collected from 1st June to 31st July 2023 using the Malaysia Medication Adherence Assessment Tool (MyMAAT) questionnaire. Multiple logistic regression analysis was performed to determine the factors associated with medication nonadherence.

Results: A total of 350 patients participated in the study. The majority of the patients were female (59.7%) and Malay (98.9%) with a mean age of 66.5 ± standard deviation of 5.2 years. A total of 187 (53.4%) the study population were nonadherent to their medications. Household income was the only variable that was significantly associated with nonadherence. Patients with household income above RM1,500 per month had lower odds of medication nonadherence (adjusted OR: 0.561; 95% CI: 0.349-0.901, *p*=0.017).

Conclusion: Half of the geriatric patients with diabetes who attended the public health clinics in Marang district were nonadherent to their medications. As low household income could be associated with medication nonadherence, further studies are needed to understand the factors behind so that strategies can be designed to improve medication adherence.

Keywords: Elderly, diabetes, medication nonadherence, medication adherence

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Introduction

In Malaysia, geriatric population is defined as individuals aged 60 years and above (1). This group has been categorised as one of the national health priorities because they were more likely to experience age-related diseases, higher morbidity, frequent healthcare service utilisation, greater risk of complications, and have a higher demand for specialised services (2). Increased life expectancy, coupled by the changes in the structure of the society, led to a growing number of elderly people living alone. Absence of family support may increase the likelihood of chronic diseases progressing both physically and mentally (3). A country with ageing population has its consequences especially related to health issues (4).

According to the 6th Edition Clinical Practice Guidelines on Management of Type 2 Diabetes Mellitus (T2DM) published in 2020, the management of diabetes involved lifestyle modification, taking medications as prescribed, and educating patients to promote empowerment and self-care. The guideline also stated an increasing prevalence of diabetes among younger individuals, with 4.3% and 5.4% among those aged between 18-19 years and 20-24 years, respectively. Despite that, the prevalence of diabetes was still highest among the elderly, with 42.4% among those age 60- 64, 43.4% among age 65-69, 40.6% among age 70-74% and 38.4% among those over 75 years old. The real burden of diabetes was due to the development of microvascular complications, for example eye and kidney disease, and macrovascular complications, such as coronary, cerebrovascular, peripheral vascular complications, which contributed to morbidity and mortality (5).

Long-term medications use was common in T2DM management. Although drugs were effective in treating diabetes, medication nonadherence was an obstacle to achieve full therapeutic benefits. The process of taking the medication as directed was defined as medication adherence (6). The issue of medication adherence was significant across all demographics and even more among the elderly (7). Almost 50% of geriatric patients with chronic conditions did not adhere to their prescribed drugs as been told by healthcare professionals (4). Low medication adherence in diabetic patients typically resulted in reduction of medication efficacy, poor clinical outcomes (in terms of glycaemic control), increased drug-related side effects, and increased social health care expenditures. Previous studies found that age, medication knowledge, the existence of comorbidities, family support, stress, satisfaction with medical care, and religious coping strategies were the factors impacting medication adherence among T2DM patients (8).

Comorbid conditions and prescription of multiple medications have been observed to reduce patients' adherence toward their medications (9). Based on a study from Iran, the percentage of patients with good adherence gradually declined as the number of comorbidities increased, from 20% in those without comorbid diseases to 11.1% in those with three to five comorbid conditions (10). Elderly patients at risk of nonadherence often had multiple comorbid conditions and were on numerous drugs (11). One of the findings from the study in Bangladesh implied that adherence significantly declined with age. In another study, 12.9% of the subjects in the 60–70 age range and 33.7% of those over 71 years old had low levels of adherence (10).

A study conducted in 2021 at the outpatient pharmacy of Sultan Ahmad Shah Medical Centre (SASMEC) in Pahang, Malaysia found that a total of 134 patients, mostly elderly (99%), returned 11,054 units of prescription medications, including pills, inhalers, insulin pens, bottles, and plastic containers, with a total value of 13,594.90 Ringgit Malaysia (RM), averaging RM101.45 per patient (12). The returning of unused medications might be one of the indicators of potential medication nonadherence. It is crucial to improve medication adherence in patients with chronic disease to reduce early mortality and social burden. Identifying the factors associated with medication adherence may guide healthcare professionals in developing interventions to improve adherence rates (8). Therefore, this study was conducted to assess the rate of medication nonadherence and to identify the factors associated with medication nonadherence among geriatric patients with diabetes mellitus at the public health clinics in Marang District.

Methods

This was a cross-sectional study among geriatric patients with T2DM who were receiving routine follow-up care at all six Ministry of Health (MOH) health clinics in Marang District, Terengganu, from 1st June to 31st July 2023. Ethical approval was obtained from the MOH Medical Research and Ethics Committee (MREC), and the study was registered in the National Medical Research Register (NMRR-23-01793-RR9).

The sample size was calculated using OpenEpi software. Considering 95% confidence interval (CI) with 5% of margin error and estimated proportion of 39.7% medication nonadherence rate in Malaysian primary care clinics (4), by allowing 20% drop out, the final sample size required was 350 geriatric patients.

Patients were recruited from the outpatient pharmacies at all six MOH health clinics in Marang District. The study included geriatric patients with T2DM who self-administered their medications and excluded those with cognitive impairment and illiteracy. Systematic random sampling was performed, in which every third patient attending outpatient pharmacy for medication collection appointments was approached and assessed for eligibility as the study participants throughout the study period. Trained pharmacists identified eligible patients that fulfilled the inclusion and exclusion criteria at the outpatient

pharmacy counter and invited them into the counselling room for further explanations about the study before recruiting them. All participants were given written and oral explanation on the purpose and methodology of the research, and confidentiality assurance. They were also assured that participation was voluntary and they could withdraw from the study at any time during the questionnaire completion without affecting their follow up at the clinic. Written informed consent was obtained prior to data collection. The questionnaire administration was guided by the trained pharmacists who underwent training about the study instrument in May 2023 to ensure consistent understanding of the questions. Each interview session lasted approximately 20 minutes.

Data were collected using a validated Malay version of Malaysia Medication Adherence Assessment Tool (MyMAAT) in which prior formal permission was obtained from the author (13). The tool comprises 12 questions that evaluate two different aspects of medication self-efficacy which were medication-taking behaviours related to nonadherence and the reasons for medication nonadherence. Each question employed five-point Likert-scale responses, ranging from ‘strongly agree’ to ‘strongly disagree’. The answers were scored, with each ‘strongly agree’ to ‘strongly disagree’ response assigned between one and five marks, respectively. A total score of 54 and above was considered good adherence, while score below 54 indicated moderate and poor adherence (13).

Data were analysed using SPSS version 27 for Windows. Categorical data were presented as frequencies (n) and percentages (%), while continuous data were presented as mean and standard deviation (SD). Simple logistic regression analysis was conducted to identify the variables associated with medication nonadherence. Variables with a *p*-value of <0.25 in the simple logistic regression were subsequently included in a multiple logistic regression model for further analysis to determine significant factors associated with medication nonadherence. The adjusted odds ratios (ORs) were presented, with a *p*-value of <0.05 considered statistically significant.

Results

A total of 420 geriatric patients were approached in this study and assessed for eligibility. Based on inclusion and exclusion criteria, the final number of respondents was 350, yielding a response rate of 83.3%. The mean ± SD age of patients was 66.5 ± 5.2 years, with the majority of them being female (59.7%), Malay (98.9%) and married (80.0%). Most of the participants completed secondary and tertiary education (51.7%), were non-employed (86.0%), and lived with family members (90.9%). Additionally, 99.1% of them had co-morbidities. The demographic data were tabulated in Table 1.

Table 1: Sociodemographic and disease characteristics of study population (n=350)

Variables	n (%)	Mean± SD
Age (year)		66.5 ± 5.2
≤ 65 years	175 (50.0)	
> 65 years	175 (50.0)	
Gender		
Male	141 (40.3)	
Female	209 (59.7)	
Ethnicity		
Malay	346 (98.9)	
Non-Malay	4 (1.1)	
Living situation		
Live alone	32 (9.1)	
Live with family members	318 (90.9)	
Educational level		
Informal / primary education	169 (48.3)	
Secondary / tertiary education	181 (51.7)	
Marital status		
Married	280 (80.0)	
Single / divorced	70 (20.0)	
Employment status		
Unemployed / retired	301 (86.0)	
Employed	49 (14.0)	
Household income (RM)		1,543.30 ± 1,996.80
≤ RM1,500	247 (70.6)	
> RM1,500	103 (29.4)	
Smoking status		
No	315 (90.0)	
Yes	35 (10.0)	
Comorbidities		
No	3 (0.9)	
Yes	347 (99.1)	
Duration of T2DM		
≤ 10 years	224 (64.0)	
> 10 years	126 (36.0)	
Number of medications		
≤ 5	160 (45.7)	
> 5	190 (54.3)	
Antidiabetic medications		
OGLD	123 (35.1)	
Insulin with or without OGLD	227 (64.9)	
Experienced side effects of medications		
No	279 (79.7)	
Yes	71 (20.3)	
Difficulties swallowing medications		
No	317 (90.6)	
Yes	33 (9.4)	

Abbreviation: T2DM = Type 2 Diabetes Mellitus; OGLD = Oral glucose-lowering drug; SD = Standard deviation

A total of 187 (53.4%) geriatric T2DM patients were categorised as having poor medication adherence with MyMAAT score less than 54, while 163 (46.6%) patients were having good adherence with MyMAAT score of 54 and higher. There was no statistically significant difference in the demographic characteristics between the medication adherence and nonadherence group, except for household income (p=0.042).

Table 2: Characteristics of adherence and nonadherence group (n=350)

Variables	Adherence, n (%) / mean ± SD (n=163)	Nonadherence, n (%) / mean ± SD (n=187)	*p*-value
Age (year)	66.88 ± 5.3	66.11 ± 5.1	0.164 [a]
≤ 65years	74 (45.4)	101 (54.0)	
> 65years	89 (54.6)	86 (46.0)	
Gender			0.344 [b]
Male	70 (42.9)	71 (37.9)	
Female	93 (57.1)	116 (62.1)	
Ethnicity			0.342 [c]
Malay	160 (98.2)	186 (99.5)	
Non-Malay	3 (1.8)	1 (0.5)	
Living situation			0.147 [b]
Live alone	11 (6.7)	21 (11.2)	
Live with family members	152 (93.3)	166 (88.8)	
Educational level			0.562 [b]
Informal / primary education	76 (46.6)	93 (49.7)	
Secondary / tertiary education	87 (53.4)	94 (50.3)	
Marital status			0.668 [b]
Married	132 (81.0)	148 (79.1)	
Single/ divorced	31 (19.0)	39 (20.9)	
Employment status			0.137 [b]
Unemployed / retired	145 (88.9)	93 (49.7)	
Employed	18 (11.1)	94 (50.3)	
Household income (RM)	1,775.2 ± 2,096.22	1,341.2 ± 1,888.5	0.042 [a, #]
≤ RM1,500	106 (65.0)	141 (75.4)	
> RM1,500	57 (35.0)	46 (24.6)	
Smoking status			0.239 [b]
No	150 (92.0)	165 (88.2)	
Yes	13 (8.0)	22 (11.8)	
Comorbidities			0.551 [c]
No	1 (0.6)	2 (1.0)	
Yes	162 (99.4)	185 (99.0)	
Duration of T2DM			0.459 [b]
≤ 10 years	101 (62.0)	123 (65.8)	
> 10 years	62 (38.0)	64 (34.2)	
Number of medications			0.238 [b]
≤ 5	80 (49.1)	80 (42.8)	
> 5	83 (50.9)	107 (57.2	
Antidiabetic medications			0.199 [b]
OGLDs	63 (38.7)	60 (32.1)	
Insulin with or without OGLD	100 (61.3)	127 (67.9)	
Experienced side effects of medications			0.106 [b]
No	136 (83.4)	143 (76.5)	
Yes	27 (16.6)	44 (23.5)	
Difficulties swallowing medications			0.892 [b]
No	148 (90.8)	169 (90.4)	
Yes	15 (9.2)	18 (9.6)	

[a] Independent t test; [b] Chi-square test; [c] Fisher's exact test; [#] statistically significant.
Abbreviation: T2DM = Type 2 Diabetes Mellitus; OGLD = Oral glucose-lowering drug; SD = standard deviation

Simple logistic regression analysis was conducted to identify the factors associated with medication nonadherence. Variables with a $p<0.25$ in simple logistic regression such as age, living situation, household income, smoking status, number of drugs, type of antidiabetic and side effects of drug were further analysed using multiple logistic regression. It was found that household income emerged as the only variable that was significantly associated with nonadherence (Table 3). Patients with a household income above

RM1,500 per month were less likely to be associated with nonadherence (adjusted OR: 0.561; 95% CI: 0.349-0.901, *p*=0.017) compared to the lower income group.

Table 3: Predictor of nonadherence among geriatric patients with diabetes mellitus (n=350)

Variables	Simple Logistic Regression			Multiple Logistic Regression [a]		
	(b)	Crude Odds Ratio (95% CIs)	p-value	(b)	Adjusted Odds Ratio (95% CIs)	p-value
Age						
≤ 65years	0	1.00		0	1.00	
> 65 years	-0.029	0.972 (0.933–1.012)	**0.164**	-0.038	0.963 (0.923-1.007)	0.075
Gender						
Male	0	1.00				
Female	0.207	1.230 (0.801-1.887)	0.344			
Ethnicity						
Malay	0	1.00				
Non-Malay	-1.249	0.287 (0.030-2.784)	0.281			
Living situation						
Live alone	0	1.00		0	1.00	
Live with family members	-0.559	0.572 (0.267-1.226)	**0.151**	-0.547	0.579 (0.264-1.271)	0.173
Educational status						
Informal / primary education	0	1.00				
Secondary / tertiary education	-0.124	0.883 (0.580-1.345)	0.562			
Marital status						
Married	0	1.00				
Single / divorced	0.115	1.122 (0.663-1.900)	0.668			
Employment status						
Unemployed / retired	0	1.00		0	1.00	
Employed	0.470	1.601 (0.858-2.985)	**0.139**	0.438	1.550 (0.822-2.922)	0.176
Household income						
≤ RM1,500	0	1.00		0	1.00	
> RM1,500	-0.500	0.607 (0.382-0.964)	**0.034**	-0.578	0.561 (0.349-0.901)	**0.017** [#]
Smoking status						
No	0	1.00		0	1.00	
Yes	0.431	1.538 (0.749-3.162)	**0.241**	0.391	1.478 (0.700-3.121)	0.306
Comorbidities						
No	0	1.00				
Yes	-0.560	0.571 (0.051-6.355)	0.649			
Duration of T2DM						
≤ 10 years	0	1.00				
> 10 years	-0.165	0.848 (0.547-1.313)	0.459			
Number of medications						
≤ 5	0	1.00		0	1.00	
> 5	0.254	1.289 (0.845-1.966)	**0.238**	0.292	1.339 (0.866-2.070)	0.189

Antidiabetic medications						
OGLD	0	1.00		0	1.00	
Insulin with or without OGLD	0.288	1.334 (0.859-2.071)	**0.200**	0.349	1.418 (0.903-2.225)	0.129
Experienced side effects of medications						
No	0	1.00		0	1.00	
Yes	0.438	1.550 (0.909-2.643)	**0.108**	0.440	1.553 (0.110-2.665)	0.108
Difficulties swallowing medication						
No	0	1.00				
Yes	0.050	1.051	0.892			

[a] Backward Multiple Logistic Regression model was applied; [#] statistically significant

Constant 2.839

Multicollinearity and interaction term were checked and not found

Hosmer-Lemeshow test, p=0.819, Classification table 57.1%; Area under ROC curve 0.59

Abbreviation: T2DM = Type 2 Diabetes Mellitus; OGLD = Oral glucose-lowering drug; CI = Confidence interval.

Discussion

In this study, the prevalence of medication nonadherence among geriatric patients with T2DM in Marang District, Terengganu was 53%. This was higher than the similar study findings reported from Muar, Johor (39.7%) (8) and Shandong province, China (19.9%) (14). Another study conducted in the state of Selangor found that up to 83.2% of their geriatric patients were not adherent to their medications as prescribed (15). These variations in the level of adherence could be attributed by the differences in data collection tools, population, healthcare systems, study design and participants' socioeconomic characteristics.

Household income was the only factor that was significantly associated with medication nonadherence among the diabetic geriatric patients in this study. Patients with monthly household income of RM1,500 and below were more likely to be nonadherent to their medications. Our findings were coherent with a previous study from Canada, where individuals with lower household income were more likely to exhibit nonadherence due to challenges in securing transportation to collect medication, along with the lack of family support compared to those in adherence groups (16,17). Financial limitations may hinder the access to necessary pharmacological therapy due to limited resources and transportation facilities to get the medications. This was particularly relevant for individuals requiring chronic medical care, such as geriatric patients with comorbidities who have regular follow-up visits to the healthcare facilities. This situation contributed to nonadherence, that could potentially lead to increased hospitalisation and additional medical costs.

Previous studies showed that patients with low economic status tend to discontinue their medications due to affordability issues (18). The costs of medications and transportation problems in low-income populations could contribute to medication nonadherence (19). Cost related nonadherence (CRNA) was reported to be common among diabetes patients, particularly when they were driven by financial stress and insecurity with healthcare (20). Although the medications provided in the Malaysia public sector health clinics were fully subsidised by the government, other costs that occur during the health services utilisation and medications collection process could hinder the patients from taking their medications as instructed (21). Therefore, the government together with non-governmental organisations (NGO) and healthcare professionals should collaborate to ensure the continuity of the treatment and reduce the risk of non-adherence.

Other characteristics such as age, gender, ethnicity, living situation, educational status, marital status, employment status, smoking status, comorbidity, duration of diabetes, number of drugs, types of antidiabetic drugs, and side effects did not show significant associations with medication nonadherence in this study. A study that was carried out in Muar, Johor also found no effect of gender on medication nonadherence (8). However, another study conducted in regional hospitals in Cameroon found that females were more likely than men to forget taking their medications, miss doses, put off filling the prescription, and request lower cost medication (22). Ethnicity was not associated with medication nonadherence in this study. However, previous study revealed that racial or ethnic differences might influence medication nonadherence

due to perceived differences in beliefs or knowledge about diabetes management (23). Education level and gender also showed no association with medication nonadherence. Similarly, a study conducted in Jordan (24) found that marital status and the presence of family members did not affect medication nonadherence among geriatric patients. Meanwhile, another study identified that external factors such as home and community environment, level of support related to these resources, and interpersonal connections, especially family support, were thought to be crucial components of a patient's resolve to take their medication as prescribed (7). Our study found that employment status was not associated with medication nonadherence, which was aligned with a previous study in China (14). Conversely, another study stated that the self-employed individual had a nearly eight-fold higher nonadherence rate, likely due to their hectic schedules and frequent travel (25)

In this cross-sectional study, the duration of diabetes treatment was not significantly associated with medication nonadherence. However, this was not consistent with another study where younger patients with shorter treatment durations showed higher medication nonadherence, typically due to insufficient understanding of the condition, apprehension about adverse effects, and the burden of following the regimens. Older patients with longer illness durations generally had greater knowledge about the condition, understood the need of glycaemic management to avoid complications, and received family support in managing their diabetes (26). In terms of difficulty in swallowing medications, our findings contrasted with a systematic review which listed difficulty swallowing medication as a factor of nonadherence. Other risk factors of nonadherence included frequent dosing, high number of prescribed medications, drug formulation and poor taste (27,28). The presence of comorbidities was another risk factor for medication nonadherence. Diabetes patients with comorbidities generally have multiple medications of different pharmacological classes such as antihypertensive, lipid-lowering agents, and antiplatelet. This complex treatment regimen could have contributed to nonadherence. However, our study found no association between the number of concurrent medications or comorbidities with medication nonadherence. A previous study in Johor also reported no association between the number of medications and medication nonadherence (8). Patients with numerous medications and complex treatment might have experienced more side effects, leading to decreased adherence (29). Hence, greater attention from healthcare professional was needed to prevent the risks of polypharmacy and increase adherence rate.

This study had several limitations. Firstly, self-reporting with guided interview was used for data collection in this study, which could have introduced biases related to social desirability and lead to recall bias. Secondly, it might be challenging to extrapolate the study's findings to other groups of patients because the study only included patients within a single health district.

Conclusion

Overall, this study found that the percentage of medication nonadherence among geriatric patients with diabetes mellitus in the Marang district health clinics was 53.4% with household income identified as the only significant factor associated with medication nonadherence. Identifying the possible factors of medication nonadherence can help pharmacists to implement strategies to enhance patients' medication adherence and improve their health outcomes.

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Conflict of Interest statement

The authors declare that there is no conflict of interest.

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Attainment of Therapeutic Vancomycin Trough Serum Concentrations with Initial Dosing in Neonatal Intensive Care Unit Patients

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Abstract

Introduction: Vancomycin is commonly used to treat neonatal late-onset sepsis. It is the first-line antibiotic for treatment of infections caused by coagulase-negative staphylococci (CoNS) and methicillin-resistant *Staphylococcus aureus* (MRSA). However, data for dosing and monitoring of vancomycin in the local neonatal population is lacking.

Objective: This study aimed to assess the percentage of neonates achieving a vancomycin serum trough concentration between 10 to 20 mcg/mL with initial vancomycin dosing.

Methods: A retrospective cross-sectional study was conducted to review the therapeutic drug monitoring serum trough levels in Hospital Kajang Neonatal Intensive Care Unit (NICU) patients who received at least 48 hours of intravenous vancomycin therapy from January 2013 to December 2018. The percentage of neonates achieving sub-therapeutic (<10mcg/mL), therapeutic (10-20mcg/mL), and supra-therapeutic (>20mcg/mL) vancomycin trough levels were compared.

Results: Of the 51 patients included, the mean gestational age was 31.8 ± 4.7 weeks whereas mean postmenstrual age was 35.3 ± 5.2 weeks. Majority of them were preterm neonates (82.4%). On average, vancomycin therapy was initiated at a mean postnatal age of 24.1 ± 20.3 days and mean weight of 1,922.5 ± 1,012.8 grams. These neonates received vancomycin for an average of 6.7 ± 2.8 days. Overall, 41.2% achieved the target vancomycin trough level, while 21.6% of trough concentrations were sub-therapeutic and 37.3% were supra-therapeutic. Supra-therapeutic trough concentrations were more often observed in the preterm group compared to term neonates (45.2% vs 0%, $p < 0.05$). Only one neonate experienced nephrotoxicity (defined as double increment of serum creatinine from baseline).

Conclusion: The current vancomycin dosing regimens used in NICU patients yielded 41.2% of therapeutic trough concentrations. Preterm neonates experienced higher occurrence of supra-therapeutic trough levels. Further studies are required to assess the optimal dosing regimen to attain therapeutic trough concentrations in this neonatal population.

Keywords: Vancomycin, trough, neonates, initial dosing, empiric dosing

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Introduction

Vancomycin is a glycopeptide antibiotic that is commonly used for empiric treatment of late-onset sepsis in the neonatal intensive care unit (NICU) (1). The most frequent pathogens responsible for late-onset sepsis in NICU patients were Coagulase negative *Staphylococcus* (CoNS) and *Staphylococcus aureus (S. aureus)* (2). The area under the curve (AUC) and minimum inhibitory concentration (MIC) of vancomycin were evaluated by multiple pharmacokinetic/ and pharmacodynamic studies in neonates. The studies demonstrated that serum vancomycin troughs of around 10 mcg/mL (range, 7 to 15 mcg/mL) for MICs of 1 mcg/mL or less may be sufficient for the treatment of the most common neonatal gram-positive infections, predominantly CoNS (3,4).

In the setting of Hospital Kajang, the initial vancomycin dosing commonly prescribed by the clinicians was based on Micromedex NeoFax Reference with the target trough level of 10 to 20 mcg/mL. Micromedex NeoFax Reference is a neonatal drug information intended for full-term babies up to 28 days of postnatal age (PNA) and preterm babies up to 44 weeks postmenstrual age (PMA). The dosing

recommendation from NeoFax suggested intravenous vancomycin 10 to 15 mg/kg every 12 or 18 hours for PMA 29 weeks or less and 10 to 15 mg/kg every 8 or 12 hours for PMA more than 30 weeks, depending on PNA (5). The subsequent dosing of vancomycin will be guided by the therapeutic drug monitoring (TDM) of serum vancomycin trough level (6).

In 2009, the consensus guidelines by the Infectious Diseases Society of America (IDSA) increased the lower limit of trough concentration from 5 to 10 mcg/mL due to the findings that exposure of *Staphylococcus aureus* to trough level of less than 10 mcg/mL can yield strains with vancomycin-intermediate *Staphylococcus aureus* (VISA). In 2011, the IDSA Methicillin-resistant *Staphylococcus aureus* (MRSA) guidelines suggested a higher trough level of 15 to 20 mcg/mL to improve vancomycin bacterial killing when treating serious MRSA infections in adults (7). Although a higher trough level was implemented, the approach of initial vancomycin dosing was not addressed (8). Given the lack of data for vancomycin efficacy and monitoring in the paediatric and neonatal population, the information was often based on data extrapolated from the adult population (9). Moreover, the current dosing practices in Malaysia were derived from literature data of Caucasian infants. The pharmacokinetic variability among these populations should be considered (10).

This study aimed to evaluate the attainment of trough vancomycin concentration between 10 to 20 mcg/mL in NICU patients with the current initial vancomycin dosing. The finding of this study will help the optimisation of vancomycin therapy in this patient group. Besides prevention of toxicity, achieving the therapeutic serum level of vancomycin is crucial in ensuring the efficacy and to avoid the development of resistance (11).

Methods

A retrospective cross-sectional study was conducted to review the therapeutic drug monitoring (TDM) records of vancomycin serum trough levels in Hospital Kajang Neonatal Intensive Care Unit (NICU) patients. The ethical approval was obtained from the Medical Research Ethics Committee (MREC), Ministry of Health Malaysia (MOH). The study was registered with the National Medical Research Register (NMRR-17-3080-39364).

All neonates who received intravenous vancomycin for at least 48 hours and had steady-state vancomycin trough concentrations records between January 2013 and December 2018 were included in this study. In the ward, vancomycin was infused at a constant rate over 60 minutes via an infusion pump. Blood samples were usually collected 30 minutes prior to the fourth or a subsequent dose of vancomycin to assess the vancomycin trough concentrations, ensuring the evaluation of steady-state concentrations as recommended by Clinical Pharmacokinetics Pharmacy Handbook (6). A minimum vancomycin therapy duration of 48 hours was required as one of the inclusion criteria to achieve steady-state serum concentration. Moreover, TDM was deemed impractical for therapy durations under 48 hours, as dose adjustments cannot be carried out unless toxicity was suspected. Repeated serum measurement such as TDM after dosing adjustment and follow-up TDM after toxic concentrations were excluded in this study. In addition, patients who had renal impairment before the initiation of vancomycin therapy were excluded. Renal impairment was defined as a serum creatinine (SCr) greater than 1.5 mg/dL (133 µmol/L) or urine output less than 1 mL/kg/hour (12). Other exclusion criteria were medical records with missing data, trough levels not drawn at steady state and inappropriate sampling time.

The TDM requests during the study period were retrieved from the TDM database while the detailed information was further retrieved from patients' records at the Medical Record Department. Data collected included demographic characteristics, vancomycin doses and administration intervals, the resultant serum trough concentrations, duration of vancomycin therapy and serum creatinine levels.

The primary study outcome was the percentage of NICU patients achieving therapeutic trough concentrations between 10 to 20 mcg/mL with initial vancomycin dosing. Trough concentrations below 10 mcg/mL were classified as sub-therapeutic while trough concentrations more than 20 mcg/mL were classified as supra-therapeutic. Additional outcome included the incidence of nephrotoxicity. Nephrotoxicity was defined as double increment of the serum creatinine from baseline.

Descriptive statistics were used to illustrate the demographic data and outcomes. Proportions were compared using Chi–Square Test of Independence. Fisher's Exact Test was used when assumptions for the Chi–Square Test of Independence cannot be met. SPSS version 21 was used for the data analysis with p–value of less than 0.05 was considered as statistically significant.

Results

A total of 132 TDM observations were obtained. Forty-eight repeated TDM results were excluded. Another 33 observations were excluded based on criteria summarised in Figure 1, leaving 51 vancomycin TDM records for analysis.

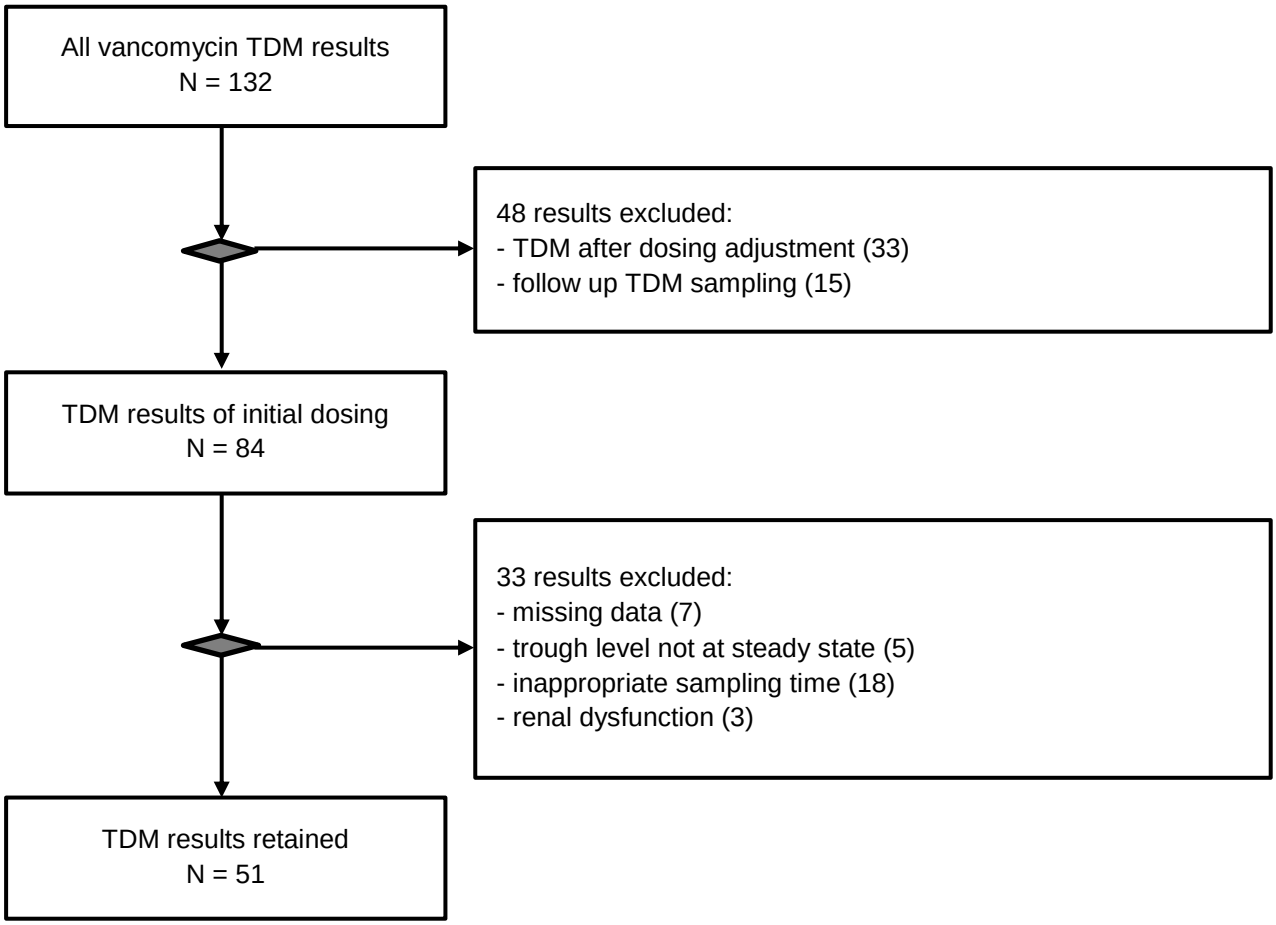

Figure 1: Flowchart of included vancomycin therapeutic drug monitoring (TDM) observations

The demographic characteristics of included patients were presented in Table 1. The mean gestational age (GA) was 31.8 ± 4.7 weeks. Preterm neonates comprised the majority of patients (82.4%), with 10 (19.6%) patients at less than 28 weeks GA, 20 (39.2%) patients were born at a GA of 28 to 32 weeks and 12 (23.5%) at a GA of 32 to 37 weeks. The mean postmenstrual age (PMA) was 35.3 ± 5.2 weeks. Majority of the neonates (76.5%) had a birth weight of less than 2500 grams, and 21.6% of neonates were small for gestational age (SGA). Small for gestational age (SGA) is defined as a birth weight of less than 10th percentile for gestational age. On average, vancomycin therapy was initiated at a postnatal age (PNA) of 24.1 ± 20.3 days with weight of 1,922.5 ± 1,012.8 grams. These neonates received vancomycin for an average of 6.7 ± 2.8 days.

The primary clinical indication of vancomycin therapy was sepsis (43.1%) as shown in Table 1. Most (76.5%) of the patients were covered with vancomycin empirically. Among twelve patients who had positive cultures, seven cultures grew MRSA (13.7% from total samples). Other cultures included *Staphylococcus aureus*, CoNS and other gram-positive bacteria.

Table 1: Demographic characteristics of patients (n=51)

Characteristics	n (%) or Mean ± SD
Gender	
Male	27 (52.9)
Female	24 (47.1)
Ethnicity	
Malay	30 (58.8)
Chinese	6 (11.8)
Indian	7 (13.7)
Foreigner	8 (15.7)
Mean gestational age (weeks)	31.8 ± 4.7
Gestational age categories	
<28 weeks	10 (19.6)
28 weeks - 31 weeks 6 days	20 (39.2)
32 weeks - 36 weeks 6 days	12 (23.5)
>37 weeks	9 (17.6)
Mean postnatal age (days)	24.1 ± 20.3
Mean postmenstrual age (weeks)	35.3 ± 5.2
Postmenstrual age categories	
≤29 weeks	8 (15.7)
30-36 weeks	24 (47.1)
≥37 weeks	19 (37.3)
Mean birth weight (g)	1,659.7 ± 936.3
Birth weight categories	
ELBW (<1,000g)	13 (25.5)
VLBW (<1,500g)	20 (39.2)
LBW (<2,500g)	6 (11.8)
≥2,500g	12 (23.5)
Mean weight at vancomycin initiation (g)	1,922.5 ± 1,012.8
SGA/AGA status	
SGA	11 (21.6)
AGA	40 (78.4)
Mean SCr at vancomycin initiation (µmol/L)	50.6 ± 17.4
Mean WBC at vancomycin initiation ($x10^3$/µl)	14.8 ± 6.3
Mean duration of antibiotic (days)	6.7 ± 2.8
Clinical indications for vancomycin therapy	
Sepsis	22 (43.1)
Pneumonia	14 (27.5)
Catheter related infection	10 (19.6)
Meningitis	2 (3.9)
Conjunctivitis	2 (3.9)
Urinary tract infection	1 (2.0)
Infection type	
MRSA	7 (13.7)
Staphylococcus aureus	1 (2.0)
CoNS	1 (2.0)
Other gram-positive bacteria (enterococcus, cellulomonas, bacillus species)	3 (5.9)
Negative blood culture	39 (76.5)

Abbreviation: ELBW = Extremely low birth weight; VLBW = Very low birth weight; LBW = Low birth weight; SGA = Small for gestational age; AGA = Appropriate for gestational age; SCr = Serum creatinine; WBC = White blood cell

With initial vancomycin dosing, only 21 (41.2%) patients achieved the target vancomycin trough concentration of 10 to 20 mcg/mL. Eleven (21.5%) patients had sub-therapeutic (less than 10 mcg/mL) trough concentrations and 19 (37.3%) were supra-therapeutic (more than 20 mcg/mL). Comparing preterm and term neonates (Table 2), 45.2% of preterm neonates had supra-therapeutic trough concentrations whereas none of the trough values from term neonates were supra-therapeutic. The percentage of sub-

therapeutic troughs were 16.7% and 44.4% for preterm and term neonates respectively. These differences were statistically significant with a p-value less than 0.05. Among neonates with PMA <37 weeks, 80% who received total daily dose (TDD) of more than 30 mg/kg/day had supratherapeutic levels compared with 31.8% who received 30 mg/kg/day or less (p <0.05).

Table 2: Achievement of vancomycin trough concentrations between preterm and term neonates and overall achievement of vancomycin trough concentrations (n=51)

Parameters	Trough levels, N (%)			p-value [a]
	<10 mg/L	10-20 mg/L	>20 mg/L	
Preterm	7 (16.7)	16 (38.1)	19 (45.2)	0.014
Term	4 (44.4)	5 (55.6)	0 (0)	
Overall	11 (21.5)	21 (41.2)	19 (37.3)	

[a] Fisher's exact tests

Table 3: Distribution of vancomycin trough concentrations with different total daily dose in neonates with PMA <37 weeks (n=32)

Total daily dose	Trough levels, N (%)			p-value [b]
	<10 mg/L	10-20 mg/L	>20 mg/L	
≤30 mg/kg/day	5 (22.7)	10 (45.5)	7 (31.8)	0.043
>30 mg/kg/day	0 (0)	2 (20.0)	8 (80.0)	

[b] Fisher's exact tests

In our study, there was one patient who was on concomitant nephrotoxin, furosemide experienced nephrotoxicity. Nephrotoxicity is defined as double increment of serum creatinine from baseline. This patient's serum creatinine increased from 52 µmol/L before initiation of vancomycin therapy to 152 µmol/L after two days of vancomycin therapy. Vancomycin was withheld due to supratherapeutic vancomycin trough concentration.

Discussion

In the neonatal population, the key factors influencing vancomycin pharmacokinetics are body weight, maturation and serum creatinine (1). Maturation of neonates is reflected by postmenstrual age (PMA), gestational age (GA) and postnatal age (PNA). Micromedex NeoFax Reference recommends vancomycin dosing based on a combination of PMA and PNA. The initial dose suggested is 10 to 15 mg/kg intravenously every 6 to 18 hours, depending on the PMA and PNA (5).

Based on the dosing recommendation from Micromedex NeoFax Reference, we found that 41.2% of patients achieved the target trough vancomycin concentration of 10 to 20 mcg/mL. A higher percentage of trough concentrations were supra-therapeutic (37.3%) compared to sub-therapeutic concentrations (21.5%). This was in contrast to several studies which reported a higher proportion of sub-therapeutic trough concentrations. Studies conducted by Ringenberg et al. and Vandendriessche et al. recorded 71.9% and 76.2% of sub-therapeutic trough concentrations, respectively. The attainment of therapeutic levels was low, 25.1% and 23.8%, respectively. Both the studies were using Micromedex NeoFax Reference as dosing regimen in their settings. It was proposed that the current dosing regimen was insufficient to yield trough levels of 10 to 20 mcg/mL (1, 13).

Our findings showed that supra-therapeutic trough concentrations were more often observed in the preterm group compared to term neonates. On the other hand, sub-therapeutic troughs were more often observed in the term neonates compared to the preterm group. This could be explained by the glomerular filtration (GFR) development in neonates. Nephrogenesis begins at the fifth week of gestation and continues until 34 to 36 weeks. In neonates born at 34 weeks of gestation or later, the development of GFR is linear. For premature neonates, the GFR development is slower (14). As vancomycin is eliminated primarily through glomerular filtration, the vancomycin elimination capacity in early days of life in premature neonates is lower, resulting in significant reduction of drug clearance (15,16).

Further analysing the distribution of vancomycin trough concentrations among neonates with PMA less than 37 weeks, the incidence of supratherapeutic levels were significantly higher in patients who received total daily dose (TDD) of more than 30 mg/kg/day compared with those who received 30 mg/kg/day

or less (80% vs 31.8%, p <0.05). The dosing recommendation from Micromedex NeoFax Reference suggested 10 to 15 mg/kg of vancomycin every 12 or 18 hours for PMA 29 weeks or less and 10 to 15 mg/kg every 8 or 12 hours for PMA 30 to 36 weeks, depending on PNA. For neonates with PMA 37 weeks and above, the dose recommended is 10 to 15 mg/kg every 6 to 12 hours, depending on PNA. The results of our study suggested that our premature neonatal population required lower dosages than the current recommendation. This could be explained by a local study conducted by Lo et al. which demonstrated that the clearance of vancomycin was lower than that estimated in the Caucasian patients. Current dosing practice was derived from literature data of Caucasian infants. Hence, it is important to consider the pharmacokinetic variability among these populations (10).

A retrospective population pharmacokinetic analysis conducted by Mehrotra et al. in 2012 assessed four different dosing regimens: based on standard weight, postmenstrual age (PMA), both postmenstrual and postnatal age (PMA/PNA), and based on serum creatinine (SCr). The study found that SCr-based dosing resulted in the least variability in predicted trough concentrations for both premature and full-term neonates. Furthermore, SCr-based dosing was the most effective in achieving trough levels of 5 to 15 mcg/mL in 63% of cases, followed by PMA/PNA-based dosing (52%), PMA-based dosing (42%), and weight-based dosing (34%) (17).

Currently, there is no consensus among the experts on the optimal dosing regimen for neonatal vancomycin (15). Developing an appropriate dosing strategy remains challenging due to the influence of multiple covariates (1), and the complex relationship between these factors and vancomycin clearance in premature neonates (10). Recently, revised consensus guidelines and reviews have recommended AUC-guided therapeutic dosing and monitoring, ideally using Bayesian estimation, to achieve the target vancomycin exposure needed for effective treatment of MRSA infections in all neonates. Monte Carlo simulations with Bayesian estimation indicated that trough concentrations between 7 and 11 mg/L are highly predictive of an AUC24 >400 mg·h/L in at least 90% of neonates. Assuming a minimum inhibitory concentration (MIC) of 1 mg/L, the guidelines suggest dosing between 10 to 20 mg/kg every 8 to 48 hours in neonates and infants up to 3 months old, depending on PMA, weight, and SCr, to achieve an AUC of 400 mg·h/L (18). Thus, an AUC24/MIC target should be considered alongside traditional trough concentration targets to minimise the risk of treatment failure and prevent vancomycin overexposure (19).

In our study, there was one (2%) incidence of nephrotoxicity from vancomycin therapy. The patient was concomitantly on furosemide. This was in accordance with a review by Lestner et al. which reported 1% to 9% occurrence of nephrotoxicity in neonates, supporting the favourable safety profile of vancomycin in neonates (20). Despite higher vancomycin trough concentrations were positively correlated with an increased risk of acute kidney injury (AKI), it was proposed that vancomycin was associated with AKI when administered concomitantly with other nephrotoxins or in other nephrotoxic disease states (21, 22).

The present study has several limitations. Because of its retrospective design, medical records that were not originally intended for research purposes were used for data collection. Also, confounders affecting vancomycin trough concentrations such as concurrent nephrotoxins and renal dysfunction were unable to be controlled. As dosing recommendations were stated in a range, different clinicians may prescribe vancomycin doses differently based on their own clinical judgement while some may be more conservative with initial dosing. Nonetheless, the study's findings may provide valuable insights for future research on optimal vancomycin dosing in neonates.

Conclusion

The current vancomycin dosing regimens used in NICU patients (10 to 15 mg/kg intravenously every 6 to 18 hours, depending on PMA and PNA) yielded 41.2% of therapeutic trough concentrations. Preterm neonates experienced higher occurrence of supra-therapeutic trough levels. Further studies are needed to determine the optimal vancomycin dosing regimen to attain therapeutic trough concentrations in this neonatal population.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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A 3-Year Review of Smoking Cessation Programme in Luyang Health Clinic, Kota Kinabalu, Sabah

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Abstract

Introduction: Quit smoking services were provided in the Ministry of Health Malaysia, health clinics and government hospitals since 2004, but the success rates have varied widely.
Objective: This study aimed to evaluate the success rate of quit smoking clinic and the association between the characteristics of patients and the success rate of the quit smoking clinic in Luyang Health Clinic, Sabah.
Methods: Participants enrolled in the smoking cessation programme between January 2017 and December 2019 at Luyang Health Clinic in Sabah, Malaysia were included in this study. Information on BMI, smoking history, quit smoking history, Fagerström Test for Nicotine Dependence, and Depression Anxiety Stress Scales (DASS) scores were collected. A patient was considered successfully quit if they remained smoke-free for six months without relapse from the agreed quit date. The characteristics of the patients, success rate and comparison between the success and the failed groups were analysed using chi square tests and independent t tests.
Results: A total of 286 patients were recruited in this study. An 8.4% success rate was achieved in the smoking cessation programme. Pregnant women had a significantly higher success rate (27.3%) compared to nonpregnant women (0%) ($p<0.001$). Additionally, the mean number of follow-up visits of 7.18 (standard deviation, SD 4.94) ($p<0.001$) among the success group were significantly higher as compared to the failed group (mean 2.95, SD 3.45).
Conclusion: Despite implementing a comprehensive smoking cessation module, there was still a high rate of unsuccessful quitters. Pregnancy status and the number of follow-up visits were associated with the success rate of smoking cessation programmes. An effective smoking cessation module that focuses on specific groups is needed to achieve a higher success rate.
Keywords: Smoking cessation, success rate, association

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Introduction

A survey conducted in 2016 in Malaysia revealed that 78.7% of adolescent smokers had started smoking before the age of fourteen. The survey also showed that 28.5% of current cigarette smokers had already developed a low dependence on nicotine (1). Smoking is the leading cause of preventable deaths in Malaysia, accounting for over 20,000 deaths each year. The economic burden of smoking in Malaysia is estimated to be over RM10 billion annually (1). Smoking damages almost all organs in the body that leads to various ailments and disabilities (2). The most efficient strategy to lower the risk of smoking-related diseases is to stop smoking. Smoking cessation programmes were provided to the public at 731 Ministry of Health Malaysia (MOH) health clinics and 46 MOH hospitals (3) throughout Malaysia. These programmes are a national programme that provides free smoking cessation services to the public.

Despite the continuation of the national programmes during the past ten years, the success rates of smoking cessation programmes have varied widely across the healthcare facilities in Malaysia. This indicated the need for a closer examination of the programme implementation and effectiveness. A study done at the Seremban district involving public healthcare clinics showed that 30.2% of patients recruited were able to quit within six months of follow up (4). Another study by Ezat et al. reported that 17.3% of patients recruited were able to quit for at least six months. This study involved patients from eight randomly chosen government primary healthcare clinics including from the states of Kedah (northern zone), Perak

(central zone), Johor (southern zone) and Kelantan (eastern zone) (5). Elderly smokers (above 40 years old), having smoked for more than 15 years, smoked less than ten cigarettes per day, had a previous history of quitting attempt, self-referral to the clinic, high confidence level, attended smoking cessation clinic at least four times, having counselling session lasted at least 30 minutes and being satisfied with the clinic service were the factors that significantly affects the success rate in this study. A similar study conducted in Taiwan found that 37.7% of patients achieved the six-month point abstinence (6). This study reported that higher success rates were associated with smoking less than twenty cigarettes per day, having a lower Fagerström Test for Nicotine Dependence (FTND) score, having lower exhaled carbon monoxide (CO) concentration value at first visit, and attending more than one smoking cessation session. Different clinic approach and measures could contribute to different success rates despite being in the same national programme.

Luyang Health Clinic is one of the primary care clinics that offer smoking cessation programmes in Sabah, Malaysia. Based on Figure 1, the standard care pathway for smoking cessation programme at Luyang Health Clinic involves a physician first referring a patient to the quit-smoking clinic. The patients will then need to make an appointment with the nurse in charge of the quit-smoking clinic. During first visit, a physician will assess the patient and set a quit date. This assessment includes evaluating the patient's body mass index (BMI), smoking history, quit smoking history, FTND score, and completing the Depression Anxiety Stress Scales (DASS) questionnaire. The FTND is used to assess a patient's nicotine dependence and can be used to guide the dosage of nicotine replacement therapy. Meanwhile, the DASS questionnaire assesses the patient's level of stress, anxiety, and depression. The smoking cessation programme consists of pharmacological and nonpharmacological methods of reducing smoking. The pharmacological method involves nicotine replacement therapy (NRTs) to control nicotine cravings, while the nonpharmacological process involves behavioural therapy counselling without using NRTs.

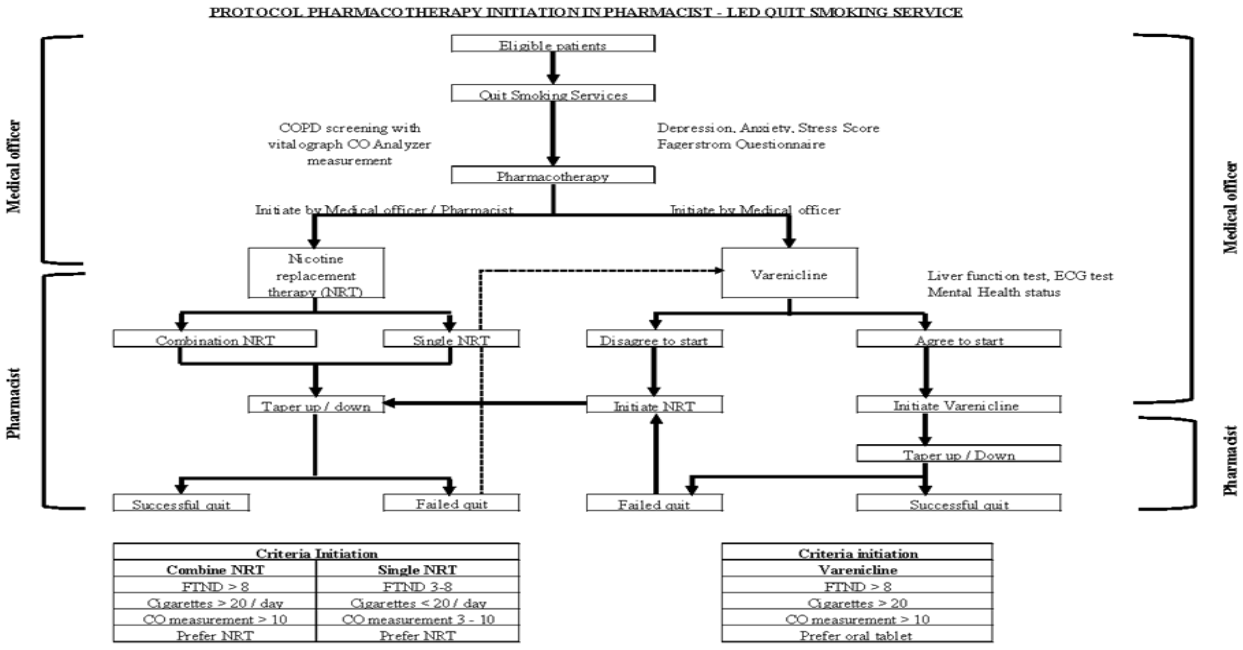

Figure 1: Protocol pharmacotherapy initiation in pharmacist-led quit smoking service

Most smokers have the perception that they can easily quit smoking (7). Some will ask whether they can quit smoking within the six months period. This study will provide detailed data on the previous success rate of this quit smoking clinic which can be used to change the patient's perceptions and educate them on the factors that influence the success rate. By gaining a better understanding of patient characteristics and programme structure such as number of follow ups needed, will help the healthcare professionals to individualise the approach and structure more successful programmes. This will increase the success rate and encourage more patients to confidently enrol in the smoking cessation programme. Therefore, we aimed to evaluate the success rate of the smoking cessation clinic at Luyang Health Clinic and investigate the association between patient characteristics and the success rate of the smoking cessation clinic.

Methods

This retrospective observational study was conducted at a primary care centre (Luyang Health Clinic) in Kota Kinabalu, Sabah using secondary data. This study was registered with the National Medical Research Registry (NMRR ID-22-00360-Z31) and was approved by the Medical Research Ethics Committee, Ministry of Health, Malaysia.

All patients who enrolled in the smoking cessation programme at Luyang Health Clinic between January 2017 and December 2019 were included in this study through universal sampling. Patients with acute psychiatric illness were excluded from this study. The sample size was calculated using Raosoft® (Sample Size Calculator; Raosoft inc) (8). Based on 95% of confidence level, 5% margin of error and total population estimation of smokers in Kota Kinabalu district, a sample size of 384 was required to obtain statistically valid results.

Patient information and smoking history details were recorded and kept in a record file. These records provided information about patient demographics, medication regimes, and laboratory parameters. A patient is considered a successful quitter if they remain smoke-free for six months without relapse from the agreed quit date (4). A Google form was created to extract the data of interest from patients' medical records including patient characteristics, smoking history, FTND score, DASS score, number and duration of follow-up visit, and pharmacological interventions.

The data were analysed using IBM Statistical Package for Social Sciences (SPSS) version 29. Demographic data were presented as frequencies (n) and percentages (%) for categorical variables. Numerical variables, for example, age, were presented as mean and standard deviation (SD). The association between the characteristics of smokers and outcome analysis were analysed using Chi Square test for categorical data and independent t-test for continuous data. A confidence interval of 95% was utilized in this study and the results were considered statistically significant when the P-value was less than 0.05.

Results

The number of patients enrolled in the smoking cessation clinic at Luyang Health Clinic during the study period was 289. Of these, 286 patients were recruited in this study with three patients excluded due to acute psychiatric illness. Among the 286 patients, the majority were male (88.1%) and the highest proportion of patients was in the age group of 31-40 years old (26.6%). Concurrent illnesses were reported by 54.8% of the participants. Most patients (40.9%) had a normal BMI, and the mean age at which participants began smoking was 18 years old, which is the legal age to purchase cigarettes in Malaysia. Almost 73% of the patients had attempted to quit smoking at least once before joining the programme. The FTND scores indicated that most patients had a medium level of nicotine dependent (49.7%). As for mental health, the patients had varying levels of anxiety, stress, and depression, with the majority falling within the normal range for each category. The mean smoking duration was 25.75 years. The outcome of the smoking cessation programme showed that 91.6% of the patients failed to quit smoking, while only 8.4% succeeded (Table 1).

Table 1: Sociodemographic characteristics of study participants (*n* = 286)

Characteristic	n (%)	Mean (SD)
Gender		
Female	34 (11.9)	-
Male	252 (88.1)	
Age (years)		44.07 (13.61)
17-30	47 (16.4)	
31-40	76 (26.6)	
41-50	75 (26.2)	
51-60	47 (16.4)	
>60	41 (14.3)	
Concurrent illness		
No	129 (45.1)	-
Yes	157 (54.9)	
BMI (kg/m^2)		
< 18.5 (Underweight)	16 (5.6)	
18.5 - 25 (Normal)	117 (40.9)	
25 - 30 (Overweight)	109 (38.1)	
≥ 30 (Obese)	44 (15.4)	
Age when started smoking (years)	-	18.26 (5.31)
Previous quit attempt		
None	78 (27.3)	
1 - 2 times	156 (54.5)	
3 - 4 times	22 (7.7)	
> 4 times	29 (10.1)	
FTND score		
High dependent level	51 (17.8)	
Medium dependent level	142 (49.7)	
Low dependent level	88 (30.8)	
Smoking duration (years)		25.75 (13.13)
Pregnant (n=34)		
No	23 (67.6)	
Yes	11 (32.4)	
Frequency of follow-up		3.05 (3.53)
Outcome		
Failed in quit smoking	262 (91.6)	
Success in quit smoking	24 (8.4)	
DASS Score (Anxiety)		
Mild	45 (15.7)	
Moderate	13 (4.5)	
Normal	184 (64.3)	
Severe	39 (13.6)	
DASS Score (Stress)		
Mild	37 (12.9)	
Moderate	24 (8.4)	
Normal	209 (73.1)	
Severe	11 (3.8)	
DASS Score (Depression)		
Mild	26 (9.1)	
Moderate	18 (6.3)	
Normal	225 (78.7)	
Severe	13 (4.5)	

Abbreviation: FTND = Fagerström Test for Nicotine Dependence, DASS = Depression Anxiety Stress Scales, SD = Standard deviation

Most of the patients' characteristics showed no statistically significant difference between the successful and failed group except for pregnancy status (Table 2). All the women that manage to quit are pregnant women (p<0.001). The success group has a significantly higher average number of visits (7.18, SD 4.94) as compared to the failed group (2.95, SD 3.45; p<0.001) (Table 3).

Table 2: Association between characteristics of smokers and outcome analysis

Variable	Failed group, *n* (%) (n=262)	Success group, *n* (%) (n=24)	p-value [a]
Gender			
Female	31 (11.8)	3 (12.5)	0.923
Male	231 (88.2)	21 (87.5)	
Age (years)			
17-30	41 (15.6)	6 (25.0)	0.683
31-40	72 (27.5)	4 (16.7)	
41-50	68 (26.0)	7 (29.2)	
51-60	43 (16.4)	4 (16.7)	
>60	38 (14.5)	3 (12.5)	
Concurrent illness			
Without concurrent illness	118 (45.0)	11 (45.8)	0.940
With concurrent illness	144 (55.0)	13 (54.2)	
Pregnant			
No	23 (74.2)	0 (0)	**<0.001**
Yes	8 (25.8)	3 (100)	
BMI (kg/m^2)			
< 18.5 (Underweight)	15 (5.7)	1 (4.2)	0.941
18.5 - 25 (Normal)	106 (40.5)	11 (45.8)	
25 - 30 (Overweight)	100 (38.2)	9 (37.5)	
30 or > (Obese)	41 (15.6)	3 (12.5)	
Previous quit attempts			
None	73 (27.9)	6 (25.0)	0.816
1 - 2 times	143 (54.6)	13 (54.2)	
3 - 4 times	19 (7.3)	3 (12.5)	
> 4 times	27 (10.3)	2 (8.3)	
FTND score			
High dependent level (7-10)	49 (18.7)	2 (8.3)	0.439
Medium dependent level (4-6)	130 (49.6)	13 (54.2)	
Low dependent level (0-3)	83 (31.7)	9 (37.5)	
DASS Score (Anxiety)			
Mild	41 (15.6)	4 (16.7)	0.107
Moderate	13 (5.0)	0 (0.0)	
Normal	168 (64.1)	20 (83.3)	
Severe	40 (15.3)	0 (0.0)	
DASS Score (Stress)			
Mild	36 (13.7)	1 (4.2)	0.091
Moderate	25 (9.5)	0 (0.0)	
Normal	190 (72.5)	23 (95.8)	
Severe	11 (4.2)	0 (0.0)	
DASS Score (Depression)			
Mild	24 (9.2)	2 (8.3)	0.332
Moderate	19 (7.3)	0 (0.0)	
Normal	206 (78.6)	22 (91.7)	
Severe	13 (5.0)	0 (0.0)	

[a] Chi Square test

Abbreviation: FTND = Fagerström Test for Nicotine Dependence, DASS = Depression Anxiety Stress Scales, SD = standard deviation

Table 3: Comparison of age when started smoking, smoking duration, and number of follow-up visits between the success and fail groups (n)

Group (n)	Mean (SD)	p-value [a]
Age when started smoking (years)		
Success (22)	16.73 (2.60)	0.079
Fail (252)	18.39 (5.46)	
Smoking duration (years)		
Success (22)	25.09 (15.68)	0.403
Fail (250)	25.81 (12.92)	
Frequency of follow-up		
Success (22)	7.18 (4.94)	**<0.001**
Fail (258)	2.95 (3.45)	

[a] Independent t-tests

Abbreviation: SD = standard deviation

Discussion

Our study demonstrated that the success rate of smoking cessation programme in Luyang Health Clinic was considerably low. Our study showed a lower success rate compared to previous studies done by Fai et al. (42.6%) (9) and Zamzuri et al. (30.2%) (10), despite using the same module of smoking cessation programmes. The study by Fai et al. found that lower cigarette intake and lower FTND scores were associated with the success in smoking cessation. Whereas in our study, we found that FTND score was not associated with the success rate. This could be due to the incomplete data on cigarette intake for some patients in our study. Additionally, the success of smoking cessation was self-reported and not confirmed by biochemical measures. Also, our study did not control for other influencing factors, such as patient's age, gender, or smoking history. The variance might result from the practice's heterogeneity or the knowledge and expertise of the smoking cessation counsellors (11). Moreover, Wee et al. observed that some smoking cessation clinics faced challenges in securing committed staff to run the programme (12). They continued by saying that all healthcare professionals must take on extra work to manage this scenario. The Australian Cancer Society, stated in their research that patients often make twelve to fourteen attempts to quit before finally giving up (13). Furthermore, according to Chaiton and colleagues, many patients may take up to 30 tries to quit smoking successfully (14).

Pregnant women were generally willing to quit smoking for the health of their baby (15). In our study, one third of the women attending the smoking cessation clinic were pregnant, and almost 30% of them were able to quit smoking. The awareness of harmful effects of smoking during pregnancy on the baby were reported to be a significant predictor of willingness to quit smoking among pregnant women (15). Psychosocial intervention was given to the pregnant mothers during the smoking cessation programme (4). Such intervention is a way to support the pregnant women to stop smoking and eventually increases the proportion of women who manage to stop (16). Thus, reinforcing the risks of smoking on both the mother and baby such as miscarriage, preterm birth, and low birth weight can motivate the women to quit smoking during pregnancy (17, 18). Although our study found that pregnancy was significantly associated with successful smoking cessation among women, the success rate was considerably low. A study in the United Kingdom demonstrated that the intention to quit smoking decreased over time as pregnancy progressed (19). Nevertheless, information on pregnancy stages were not collected in our study. National level studies can be carried out in Malaysia to understand the quitting behaviours and intentions among smoking pregnant women so that more targeted interventions can be formulated.

Our study showed that participants with more follow-up visits had significantly higher success rate of smoking cessation. This was probably because patients who received proper advice on managing withdrawal symptoms from the trained healthcare professionals were more motivated to quit smoking. The healthcare professionals in quit-smoking clinics were trained using proper modules. This was also proved by Huang et al., where patients who attended multiple smoking cessation consultations or were treated by experienced physicians in quit-smoking clinics had higher success rates (6). A study by Xie et al. also found that smoking cessation clinics and frequent telephone follow-ups improved the success rates of quitting smoking in China (20). Thus, all healthcare professionals should be educated and updated on the harmful effects of tobacco and motivational counselling, and their roles in ensuring patient success in quitting smoking and being free from nicotine addiction (21).

Quitting smoking may be more challenging nowadays than in previous years due to the growing availability of e-cigarettes on the market. E-cigarettes are often marketed as a safer alternative to smoking, and were perceived as a tool to "quit smoking" without actually quitting nicotine. However, e-cigarettes can be just as addictive as cigarettes, and can make it harder to quit smoking as they deliver nicotine similarly to traditional cigarettes and can trigger cravings. Additionally, e-cigarettes can make it harder to resist the urge to smoke because they are more convenient and discreet than cigarettes. A study published in Tobacco Control found that quit attempters who used e-cigarette as an aid had a lower 12+ month cigarette abstinence rate than those who did not (22). Another study, published in "Pediatrics", found that teens who used e-cigarettes were more likely to start smoking cigarettes and become regular smokers than teens who did not use e-cigarettes (23). These studies suggested that e-cigarettes were not effective smoking cessation tool and could make quitting more difficult.

Our study had several limitations that should be considered. Firstly, the sample size was small, with only 24 participants who successfully quitted smoking and 262 participants who did not. It was difficult to make judgments about the effectiveness of the smoking cessation programme given the small sample size. Next, the relatively short follow-up period of six months may not be sufficient to capture potential relapses or sustained abstinence beyond this time frame. A more extended follow-up period would provide a more comprehensive understanding of the programme's effectiveness. We also encountered recording bias, as some case records were incomplete or difficult to read. Additionally, as reported in a previous study by Ismail et al., the possibility of Hawthorne effect existed, as the quit smoking status in the patients' records were collected through direct interviewed by the healthcare professional (11).

Conclusion

Our study demonstrated a high rate of unsuccessful smoking quitters among patients who attended the smoking cessation clinic at Luyang Health Clinic. Pregnancy status was significantly associated with the success rate of smoking cessation in women, highlighting the need for comprehensive measure to increase the success rate among pregnant women. The number of follow-up visits was also associated with the success of smoking cessation. Healthcare professionals should try to optimise the number of follow-up visits to improve the outcomes of the smoking cessation programme. Further research involving larger sample sizes, the use of biochemical measures, and extended follow-up periods are necessary to validate these findings.

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Conflict of interest statement

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