

PREVALENCE AND DETERMINANTS FOR INSULIN THERAPY REFUSAL AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN PRIMARY HEALTHCARE FACILITIES IN EAST COAST REGION OF PENINSULAR MALAYSIA.

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ABSTRACT

Background: Diabetes mellitus is one of public health concerns in Malaysia. Insulin therapy refusal is getting prevalent among Malaysian diabetic patients due to various attributes. The purpose of this study was to determine the prevalence of insulin therapy refusal among type 2 diabetes patients and to determine its associated factors.

Materials and Methods: A cross-sectional study was conducted from August 2015 to February 2016 in four selected health clinics in East Coast Region of Peninsular Malaysia. Diabetic patients who fulfilled the study criteria were recruited. Descriptive statistics, simple and multiple logistic regressions were used for data analysis.

Result: A total of 460 patients were recruited in this study. The prevalence of patients refused insulin therapy was 15.0%. The mean (\pm SD) age of patients refusing insulin therapy was 59.93 (\pm 1.13) year old. Majority of insulin-refusing patients were female (76.8%), Malay (81.1%) and attained secondary education level (50.7%). The mean (\pm SD) duration of diabetes among insulin-refusing patients was 7.5 (\pm 0.49) year. Majority of insulin-refusing patients had co-morbidities (84.1%) and diabetic complication (76.8%). Male gender, Malay ethnicity, duration of having diabetes and presence of diabetic complications were the significant associated factors for refusing

insulin therapy with an adjusted odds ratio (AOR) of 2.41 (95%CI: 1.37,4.26; $p=0.002$), 4.17 (95%CI: 2.27,7.66; $p<0.001$), 0.92 (95%CI: 0.87,0.97; $p=0.003$) and 3.50 (95%CI: 1.37,8.98; $p=0.009$), respectively.

Conclusion: Insulin therapy refusal is quite common in Malaysia. More proactive actions from healthcare providers needed in accordance to the pinpointed factors in order to attain better insulin therapy acceptance among diabetic patients.

Keywords: insulin therapy refusal, prevalence, type 2 diabetes mellitus, associated factors.

1.0 Introduction

Type 2 diabetes mellitus results from the body's ineffective use of insulin. Type 2 diabetes comprises the majority of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity. The incidence of diabetes mellitus is increasing worldwide. The number of people with diabetes has risen to 422 million in 2014 and it is a major cause of various complications such as blindness, kidney failure, heart attacks, stroke and lower limb amputation (World Health Organization, 2018). As for Malaysia, the overall prevalence of diabetes mellitus among adults aged 18 years old and above increased substantially from 15.2% in 2011 to 17.5% in 2015 (Institute for Public Health, 2011; Institute for Public Health, 2015).

When managing type 2 diabetes mellitus, the general focus is mainly on achieving and maintaining good glycemic control while minimizing the potential for adverse events such as hypoglycemia. Management of diabetes is complicated by the progressive nature of the disease; as β -cell function diminishes, oral hypoglycemic agents alone are frequently insufficient for maintaining glycemic control and insulin therapy is required (Wright *et al.*, 2002). Although most providers agree that insulin is an efficacious approach to the management of type 2 diabetes, many still consider insulin therapy as the last resort and indicate that their patients are hesitant to take insulin (Ghadiri-Anari *et al.*, 2013). Insulin therapy refusal is currently one of the main challenges in managing diabetic patients in Malaysia who have suboptimal control (Tan *et al.*, 2015).

A study conducted in the USA showed that 33% of type 2 diabetic patients were unwilling to use insulin therapy (Larkin *et al.*, 2007), while another study conducted among Bangladeshi patients found 42.5% of patients with type 2 diabetes unwilling to start insulin therapy initially, with 20.3% refusing insulin use even after repeated counselling (Khan *et al.*, 2008). Meanwhile, two previous local studies reported the prevalence of insulin therapy refusal in Malaysian settings were 50.7% (Azmiyah *et al.*, 2011) and 74.2% (Tan *et al.*, 2015).

In this study, we sought to determine the prevalence of insulin therapy refusal among diabetic patients and determine the factors associated with insulin therapy refusal. There are many socio-demographic and clinical factors that contributed to the refusal of insulin therapy among type 2 diabetes patients. The known socio-demographic factors contributing to insulin therapy refusal are

older age (Azmiah *et al.*, 2011; Polonsky *et al.*, 2005; Tan *et al.*, 2015), female (Nam *et al.*, 2010; Polonsky *et al.*, 2005; Tan *et al.*, 2015), low education level (Khalili *et al.*, 2016; Mostafavian *et al.*, 2018), Malay ethnicity (Azmiah *et al.*, 2011; Tan *et al.*, 2015), married (Khalili *et al.*, 2016), unemployed (Khalili *et al.*, 2016; Tan *et al.*, 2015) and no social support (staying alone) (Garay-Sevilla *et al.*, 1995). Known clinical factors associated with insulin therapy refusal include longer duration of having diabetes (Mostafavian *et al.*, 2018; Tan *et al.*, 2015), poor diabetic control (high glycated haemoglobin or HbA1c level) (Tan *et al.*, 2015), high body mass index (BMI) (Donnelly *et al.*, 2007) and presence of diabetic complications (Nam *et al.*, 2010). We expect that the findings of our study could provide important insight to healthcare providers in mitigating insulin therapy refusal at their respective healthcare facilities.

2.0 Materials and Methods

From August 2015 until February 2016, we conducted a comparative cross-sectional study in four selected primary healthcare facilities in the East Coast Region of Peninsular Malaysia. The clinics involved were Selising Health Clinic in Kelantan state; Marang Health Clinic in Terengganu state; Jaya Gading and Beserah Clinics in Pahang state. The reference populations were all type 2 diabetes mellitus patients who started on oral hypoglycemic agents (OHA) after initial diabetes diagnosis, and the study samples were all type 2 diabetes mellitus patients who fulfilled study inclusion and exclusion criteria in the four selected health clinics. The inclusion criteria were adult patients aged 18 and above, were offered insulin after failed OHA therapy, on regular clinic visits for more than 6 months and had HbA1c level of more than 8 mmol/l. Patients who were illiterate, pregnant, offered with insulin therapy immediately after initial diagnosis, and had diabetic emergencies were excluded from the study.

The sample size was calculated for each variable of associated factors for insulin therapy refusal among diabetic patients using power and sample size calculation software (Dupont and Plummer Jr, 1990) as well to compare two independent proportions. The largest estimated sample for each group was 230 using the proportion of insulin-accepting group by the factor of female (0.77) (Mostafavian *et al.*, 2018), an estimated proportion of 0.64, 5% type 1 error, 80% power and additional of 20% missing data. Therefore, the total sample size required is 460 patients.

Data were collected from patient's outpatient cards and personal diabetic follow-up record book and recorded in patient's proforma. The retrieved information includes socio-demographic data (age, ethnicity, gender, marital status, education level, occupation, working hour and social support) and clinical data (duration of diabetes since diagnosis, BMI, HbA1c level, presence of comorbidities and presence of diabetic complications). Using patient's outpatient cards and personal diabetic follow-up record book, we found a total of 596 diabetic patients who fulfilled the study criteria. From these 596 samples, a total of 460 samples were included in this study in which 391 samples obtained via simple random sampling for insulin-accepting group and only 69 samples available for insulin-refusing group.

We defined presence of comorbidities as having at least one type of comorbidities either hypertension and/or dyslipidaemia. Presence of diabetic complication was defined as having at least one of the following complications; retinopathy, nephropathy, neuropathy, coronary heart disease, cerebrovascular disease, diabetic foot and sexual dysfunction (Ministry of Health, 2015). Good social support is defined as living with family members or spouse, meanwhile poor social support referred to living alone (Garay-Sevilla *et al.*, 1995).

Data were analyzed by using SPSS software version 20. After checking the sample sets of the investigated values for the Kolmogorov-Smirnov distribution normality, it was revealed that the distribution of the investigated parameters were of normal distribution, that is why the methods of parametric statistics with mean and standard deviation calculation were used in the descriptive statistics besides frequency and percentages. Simple and multiple logistic regression analysis were used to determine factors associated with insulin therapy refusal among type 2 diabetes mellitus patients. All significant variables with a p-value <0.25 from univariable analysis and clinically important variables were chosen for multiple logistic regression analysis. A p-value <0.05 was considered statistically significant.

3.0 Result

A total of 460 type 2 diabetic patients were recruited in this study. The proportion of diabetic patients refused for insulin therapy was 15.0%. The mean (\pm SD) age was 59.93 (\pm 1.13) year old. Socio-demographically, majority of insulin-refusing patients were female (76.8%), Malay (81.1%) unemployed/housewife (82.6%), widow/widower (56.5%), worked in shift system (15.9%), attained secondary education level (50.7%) and had poor social support (56.5%). Details are shown in Table 1.

Table 1: Socio-demographic characteristics of patients in accordance to their insulin therapy outcomes (n=460)

Characteristics	Frequency (%)	
	Insulin-accepting patients (n=391)	Insulin-refusing patients (n=69)
Age (years)*	59.81 (\pm 0.51)	59.93 (\pm 1.13)
Gender		
Male	153 (39.2)	16 (23.2)
Female	238 (60.8)	53 (76.8)
Ethnicity		

Others	37 (9.5)	13 (18.9)
Malay	354 (90.5)	56 (81.1)
Education level		
Tertiary	178 (45.5)	16 (23.2)
Secondary	165 (42.2)	35 (50.7)
Primary	33 (8.4)	6 (8.7)
None	15 (3.9)	12 (17.4)
Occupation		
Unemployed/housewife	316 (80.8)	57 (82.6)
Working	75 (19.2)	12 (17.4)
Working hour		
Not applicable	316 (80.8)	57 (82.6)
Office hour	46 (11.8)	1 (1.4)
Shift system	29 (7.4)	11 (16.0)
Marital status		
Married	96 (24.6)	30 (43.5)
Single	8 (2.0)	0 (0.0)
Widow/widower	287 (73.4)	39 (56.5)
Social support		
Good	298 (76.2)	30 (43.5)
Poor	93 (23.8)	39 (56.5)

*Mean (\pm SD)

As for clinical factors, the mean (\pm SD) duration of diabetes, BMI and HbA1c among insulin-refusing patients were 7.55 (\pm 0.49) year, 27.97 (\pm 0.63) kg/m² and 10.36 (\pm 0.22) % respectively. Majority of insulin-refusing patients had co-morbidities (84.1%) and diabetic complications (76.8%). Details are shown in Table 2.

Table 2: Clinical characteristics of patients in accordance to their insulin therapy outcomes (n=460)

Characteristics	Frequency (%)	
	Insulin-accepting patients (n=391)	Insulin-refusing patients (n=69)
Duration (years) of diabetes from initial diagnosis*	10.05 (± 0.32)	7.55 (± 0.49)
BMI (kg/m²)*	27.57 (± 0.28)	27.97 (± 0.63)
HbA1c (%)*	10.74 (± 0.09)	10.36 (± 0.22)
Presence of co-morbidities		
No	99 (25.3)	11 (15.9)
Yes	292 (74.7)	58 (84.1)
Presence of diabetic complications		
No	54 (13.8)	16 (23.2)
Yes	337 (86.2)	53 (76.8)

*Mean (\pm SD)

Variables with $p < 0.25$ in the univariable analysis were gender, ethnicity, education level, working hour, social support, duration of diabetes, presence of co-morbidities and diabetic complications. Multiple logistic regression analysis revealed male gender, Malay ethnicity, duration of having diabetes and presence of diabetic complication were the significant associated factors for refusing insulin therapy among type 2 diabetic patient (Table 3).

Table 3: Factors associated with insulin therapy refusal among type 2 diabetic patients in health clinics in East Coast Region of Peninsular Malaysia (n=460).

Factors	β	S.E.	Wald statistics (df)	Adjusted OR (95% CI)	p-value
Gender					
Female				1.00	
Male	0.88	0.29	9.24 (1)	2.41 (1.37, 4.26)	0.002*
Ethnicity					
Others				1.00	
Malay	1.43	0.31	21.20 (1)	4.17 (2.27, 7.66)	<0.001*
Duration (years) of diabetes from initial diagnosis					
	-0.08	0.03	8.89 (1)	0.92 (0.87, 0.97)	0.003*
Diabetic complications					
No				1.00	
Yes	1.25	0.48	6.81 (1)	3.50 (1.36, 8.98)	0.009*

*p-value <0.05. Forward LR method applied.

No multicollinearity and no interaction found.

Hosmer Lemeshow test, p-value=0.401.

Classification table 85% correctly classified.

Area under Receiver Operating Characteristics (ROC) curve was 89.3%.

4.0 Discussion

The prevalence of insulin therapy refusal among type 2 diabetic patients in health clinics in East Coast Region of Peninsular Malaysia was 15.0%. Our finding is substantially lower than the findings from other local studies done in health clinics in Kedah state; and Federal Territories of Kuala Lumpur and Putrajaya with 50.7% and 74.2% respectively (Azmiyah *et al.*, 2011; Tan *et al.*, 2015). East Coast Region of Peninsular Malaysia is regarded as less urban region as compared to Federal Territories. Higher prevalence of insulin therapy refusal in urban areas could be attributed to the facts that urban patients prefer taking treatment from private facility without proper follow-up and care; and they usually perceived lack of satisfaction with doctor-patient relationship (Venkatesan *et al.*, 2018).

In our study, the mean age of patients refused for insulin therapy (59.93 years) was slightly higher than mean age of patients refusing insulin in Federal Territories (54.5 years) and Kedah (56.4 years) studies (Azmiah *et al.*, 2011; Tan *et al.*, 2015). Both Azmiah *et al.* (2011) and Tan *et al.* (2015) also demonstrated Malay patients as the most common insulin-refusing patients in health facilities which are similar to our finding. As for gender, majority of patients who refused for insulin therapy in our study were female which is congruent to few local and international studies (Nam *et al.*, 2010; Polonsky *et al.*, 2005; Tan *et al.*, 2015). Besides that, findings on marital status, educational level and employment status also show high degree of similarity with studies in other settings (Azmiah *et al.*, 2011; Khalili *et al.*, 2016; Mostafavian *et al.*, 2018; Tan *et al.*, 2015). Descriptively, many of our patients who refused insulin therapy worked according to shift system which is in line with a study done in Thailand (Manodpitipong *et al.*, 2017). And for social support, our finding showed good agreement with a Mexican study where majority of people who did not adhere to insulin therapy had poor family and social support (Garay-Sevilla *et al.*, 1995).

The mean duration of diabetes since diagnosis of insulin-refusing patients in our study (7.5 years) is relatively longer than the finding in Kedah state which was 5.3 years and our insulin-refusing patients also demonstrated higher mean HbA1c level (10.36%) as compared to patients in Kedah which was only 8.79% (Tan *et al.*, 2015). As for mean BMI level, our finding (27.97 kg/m²) among insulin-refusing group was much lower than a Scottish study (30.0 kg/m²) (Donnelly *et al.*, 2007). Our findings are contradictory with findings from Nam *et al.* (2010) in which higher proportion of our insulin-refusing patients had co-morbidities and diabetic complications.

We found a significant association between male gender and insulin therapy refusal. This finding is in line with a study conducted in Kubang Pasu district, Kedah where men were more likely to refuse insulin (odds ratio 1.21) as compared to women (Tan *et al.*, 2015). Possible reason could be due to male patients are normally preoccupied with routine work, daily activities and other engagements and subsequently making them more exposed to non-adherence of medication (Atinga *et al.*, 2018). However, in contrast to our finding, many international studies demonstrated that female diabetic patients were more likely to refuse insulin (Khalili *et al.*, 2016; Mostafavian *et al.*, 2018; Nam *et al.*, 2010). This finding could be explained by husbands' dominance in limiting their wives' autonomy in making healthcare decision, in which the wives do not have the final say for obtaining own healthcare such as in getting insulin therapy (Woldemicael and Tenkorang, 2010).

The result of this study showed that Malay diabetic patients had higher odds to refuse insulin but it is contradictory to finding by Tan *et al.* (2015) in Kedah. A qualitative exploration among predominantly Malay respondents reported that they perceived the need for insulin injection as social embarrassment and stigma and would lead to lifestyle restriction. Moreover, they perceived insulin injection as inconvenient and impractical to do (Hassan *et al.*, 2013).

We also found a significant association between duration of diabetes with insulin therapy refusal. Patients who had diabetes for a longer time were less likely to refuse insulin injection which is in line with finding from a study in Scotland (Donnelly *et al.*, 2007). Chronic diabetic patients had poorer adherence to oral hypoglycemic medication particularly those who required different types

of medication and frequent dosing. They perceived insulin injection as more convenient and require less frequent intake than oral hypoglycemic medication (Donnelly *et al.*, 2007).

In this current study, the presence of diabetic complications is significantly associated with insulin therapy refusal which is similar to a study finding in London (Khan *et al.*, 2008). Patients with diabetic complications had the perceptions that the requirement for insulin was an indicator of a more serious stage of their condition and commencing insulin would lead to early death (Khan *et al.*, 2008).

There were some limitations in this study. This study was done in four health clinics only, hence the findings would not be representative enough of the whole East Coast region of Peninsular Malaysia. Moreover, only patient-centered problems were elicited in this study. Medical professional and clinic setting problems were not studied.

5.0 Conclusion and recommendation

In summary, insulin therapy refusal was quite common among the patients with type 2 diabetes mellitus in East Coast region of Peninsular Malaysia; the prevalence of insulin therapy refusal was 15.0%. Male gender, Malay ethnicity, shorter duration of having diabetes and presence of diabetic complication were the significant associated factors for refusing insulin therapy among type 2 diabetes patients. As those factors are heavily intertwined with misconceptions about insulin use, more educational interventions should be carried out by healthcare providers to dispel patients' fears and erroneous beliefs and help them to start insulin therapy.

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Declaration

The authors declare that this manuscript has never been published in any other journal.

Authors contribution

Author 1,3,4,5: information gathering, data entry, technical and logistic supports.

Author 2: data analysis, manuscript drafting, editing and review.

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