

ORIGINAL ARTICLE

Insulin Therapy Refusal among Insulin-naïve Type II Diabetes Mellitus Patients in Segamat

Lee Ley Chen¹, Saodah Yaacob², Tey Keat Ming³

¹ Pharmacy Unit, Klinik Kesihatan Jementah, Jalan Muar, Kampung Gelugor 85200, Segamat, Johor.

² Pharmacy Unit, Klinik Kesihatan Palong Timur, 85000 Batu Anam, Segamat, Johor.

³ Pharmacy Unit, Klinik Kesihatan Buloh Kasap, Jalan Tasik Alai, 85010 Segamat, Johor.

ABSTRACT

Introduction: The prevalence of diabetes shows an increasing trend in Malaysia. Insulin is effective towards glycaemic control, but refusal of insulin by type 2 diabetes mellitus (T2DM) patients delay initiation of insulin therapy. This study assessed the prevalence and predictors of insulin refusal among insulin-naïve T2DM patients under all public health clinics in Segamat. **Methods:** This was a multi-centre, cross-sectional study conducted in 11 public health clinics in Segamat. Data were collected from September until November 2019 by systematic random sampling using a validated self-administered questionnaire. Factors associated with reluctance to use insulin were examined using logistic regression. **Results:** Out of 295 insulin-naïve T2DM patients recruited in this study, 234 (79.3%) rejected insulin treatment. The two foremost reasons were being unconfident of injecting insulin (83.3%) and feeling of failure to control the disease (82.1%). Educational background and gender were significantly associated with insulin treatment refusal. Patients with no formal or only primary education were found to be 1.97 times more likely to refuse insulin (adjusted OR 1.97, 95% CI 1.09-3.56, $p=0.025$), and female patients were 1.82 times more likely to refuse insulin therapy than male patients (adjusted OR 1.82, 95% CI 1.02-3.22, $p=0.041$). **Conclusion:** The prevalence of insulin refusal is high in public health clinics in Segamat. Besides counselling, intervention steps should be taken to improve insulin acceptance by targeting the most typical reasons for insulin refusal in our setting.

Keywords: Insulin-naïve type 2 diabetes mellitus, Insulin refusal, Primary care

Corresponding Author:

Tey Keat Ming, Bachelor of Pharmacy (Hons)

Email: keatming_tey@yahoo.com

Tel: +607-9441241

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterised by chronic hyperglycaemia due to inadequate insulin secretion or insulin insensitivity, or both, by the human body (1). When food (carbohydrate) is broken down, it provides glucose as fuel/energy for cells throughout the whole body. Once the food is digested, the glucose level in the bloodstream will rise. The pancreas will produce insulin, and insulin will enable glucose to be taken up by cells. Insufficient insulin secretion or insulin resistance, or both, will lead to an inability of glucose taken up by cells, causing hyperglycaemia. Type 2 diabetes mellitus (T2DM) is usually due to insulin resistance. The risk factors for T2DM are family history (genetic inheritance), age, physical activity, race/ethnicity, and diet (2,3). Chronic hyperglycaemia in the long term will lead to macrovascular and microvascular complications such as peripheral vascular disease, stroke, coronary artery

disease, retinopathy, neuropathy, and nephropathy (1).

In Malaysia, diabetes mellitus prevalence among Malaysians aged 18 years old and above had increased from 17.5% in 2015 (4) to 18.3% in 2019 (5). Among the three major ethnic groups in Malaysia, Indian has the highest prevalence of 32.4%, followed by Malays (21.6%) and Chinese (15.1%) (5). According to the National Diabetes Registry, only 32.4% of the population in Malaysia achieve adequate glycaemic control with $HbA1c < 6.5\%$ in the year 2019 (6).

The treatment goals for T2DM patients are to ensure adequate glycaemic control and prevent or slow down the progression of macrovascular and microvascular complications. Suboptimal glycaemic control was associated with increased risks of cardiovascular disease and all-cause death (7). There are several approaches to manage T2DM patients in terms of glycaemic control. Lifestyle modification in terms of medical nutrition therapy and physical activity is the first step and the mainstay therapy for T2DM patients. Oral anti-diabetes medication will be the next step if lifestyle modification is insufficient in controlling glycaemic levels. However,

due to the progression of T2DM over time, oral anti-diabetes medications with optimal doses become less potent to ensure adequate glycaemic control. Hence, insulin therapy will be the next step in managing T2DM (3,8). Although insulin therapy has been proven to be efficacious, and most T2DM patients require insulin at some point during the course of their disease, its initiation is always delayed. Studies showed that delayed insulin therapy initiation in patients with uncontrolled T2DM subsequently resulted in worse glycaemic control (9, 10).

About 29.9% of insulin-naïve T2DM patients in Western countries were reluctant to initiate insulin (11). The figure was higher in Asian countries, ranging from 50.7% to 74.2% (12-14). The negative attitude towards insulin treatment remains a primary challenge in managing the uncontrolled T2DM patients, and it was found that insulin-naïve diabetes patients had a significantly greater negative perception toward insulin treatment than those already on insulin therapy (15).

The study assessed the prevalence and predictors of insulin refusal among follow-up insulin-naïve T2DM patients in 11 public health clinics in Segamat. Patients from rural areas might have different perceptions about the healthcare of T2DM compared to those from an urban setting. By understanding the factors associated with insulin therapy refusal, effective intervention can be designed to overcome the negative perceptions of patients towards insulin therapy in rural communities. The burden of diabetic complications can be lowered, and patient's quality of life can be improved if more patients were successfully started on insulin therapy earlier.

MATERIALS AND METHODS

This research is registered with the Malaysian National Medical Research Register with ID: NMRR-19-1086-47850(IIR) and approved by the Medical Research and Ethics Committee of the Ministry of Health Malaysia.

Subject and Setting

This multi-centre, cross-sectional study was conducted in all 11 public health clinics under Pejabat Kesihatan Daerah Segamat (PKD Segamat). Data collection was carried out from 1st September 2019 to 30th November 2019. Insulin-naïve T2DM patients aged 18 years and above were recruited using systematic random sampling during the study period. Gestational diabetes mellitus patients, walk-in patients, patients who cannot understand Malay or English, patients with mental disorders, and patients unwilling to participate in this study were excluded.

Sample Size

Sample size estimation was determined using the single proportion formula. According to Tan et al., the prevalence of patients who refused insulin treatment

was 74.2% (14). The sample size needed was 295 based on calculations with a confidence interval of 1.96 and a precision of 0.05. An additional 20% was added into the sample to incorporate the dropout rate. Thus, the estimated total sample size was 369 in total. Each clinic was assigned a specific number of required samples proportionate to the number of patients in each health clinic.

Study Design

Trained pharmacists conducted data collection in each clinic during the study period. All the pharmacists were trained to handle the assessment process in the same manner to reduce the risk of assessment bias. Patients who met all inclusion criteria were recruited throughout the data collection period using systematic random sampling where every third patient was selected. An information sheet was given to every participant, and consent forms were signed. A self-administered questionnaire was used for this study. The questionnaire had two parts of information to be filled in by the participants. The first part of the questionnaire recorded the participants' demographic data (i.e. age, gender, ethnicity, marital status, education level, employment status, and income). The second part concerned the clinical data (i.e. duration diagnosed with T2DM, current treatment, and recent HbA1c level) and patients' perception on insulin therapy. HbA1c level was obtained by data collectors in each clinic through patients' medical records. Patients who refused insulin therapy were required to answer 12 closed-ended questions to determine why they refused insulin treatment. The original questionnaire was developed by Nur Azmiah et al. and later modified by Tan et al. with Cronbach's alpha value of 0.745 (12,14). This study used the version developed by Tan et al without any modification. Both authors' permissions were obtained for the usage of the questionnaire.

Statistical Analysis

The data were analysed using descriptive and inferential statistics with the SPSS version 18 software. For inferential statistics, an independent t-test and the Pearson chi-square test were performed to compare the two groups of continuous data and to test the association of two categorical data, respectively. Factors that may predict insulin therapy refusal were examined using simple logistic regression and multiple logistic regression. The results were significant if $p < 0.05$.

RESULTS

A total of 327 respondents were recruited in this study. Thirty-two respondents were excluded due to incomplete demographic data or without HbA1c level, or both, resulting in 295 final respondents with complete data. The mean age of 295 respondents was 59.7 ± 9.7 years, with a mean diagnosis of T2DM duration of 6.8 ± 5.3 years and a mean HbA1c level of $7.5\% \pm 1.4\%$. Most of

the respondents were females (57.6%), Malays (65.4%) and married (88.8%).

The prevalence of patients who rejected insulin treatment was 79.3% (Table I). There were significantly more females (83.5%) and respondents with lower educational levels (85.0%) who refused insulin therapy. As shown in Table II, the top three reasons for insulin therapy refusal were being unconfident of injecting insulin (83.3%), followed by the feeling of failure to control diabetes mellitus (82.1%), and not showing any symptoms of poorly controlled diabetes mellitus (79.5%).

Table I: Demographic data according to acceptance of insulin therapy

Demographic	Accept	Refuse	P-value
N (%)	61 (20.7%)	234 (79.3%)	-
Mean Age, years	58.3	60.1	0.199*
Gender			
Male (%)	33 (26.4%)	92 (73.6%)	0.042#
Female (%)	28 (16.5%)	142 (83.5%)	
Year of Diagnosis, years	6.56	6.91	0.650*
Race			
Malay	38 (19.7%)	155 (80.3%)	0.564#
Non-Malay	23 (22.5%)	79 (77.5%)	
Mean HbA1c, %	7.52	7.54	0.920*
Education			
Tertiary & Secondary	40 (25.8%)	115 (74.2%)	0.022#
Primary & no formal	21 (15.0%)	119 (85.0%)	
Income			
≤RM2000	40 (22.3%)	139 (77.7%)	0.379#
>RM2000	21 (18.1%)	95 (81.9%)	
Employment Status			
Employed	52 (20.1%)	207 (79.7%)	0.494#
Unemployed	9 (25.0%)	27 (75.0%)	

*independent t-test
chi-square test

Table II: Reasons for insulin refusal among the patients with T2DM in Segamat

Reason for insulin therapy refusal	Agree, n (%)	Disagree, n (%)
Unconfident of injecting insulin	195 (83.3)	39 (16.7)
Failure of controlling your type 2 diabetes mellitus	192 (82.1)	42 (21.9)
Do not show any symptoms of poorly controlled diabetes mellitus	186 (79.5)	48 (20.5)
Fear of pain upon injecting insulin	178 (76.1)	56 (23.9)
Fear of complications such as renal failure and blindness	164 (70.1)	70 (29.9)
Insulin therapy will cause life and work restrictiveness	163 (69.7)	71 (30.3)
Fear of hypoglycemia	152 (65.0)	82 (35.0)
Increase in financial burden	133 (56.8)	101 (43.2)
Vision problem	88 (37.6)	146 (62.4)
Lack of family members support	76 (32.5)	158 (67.5)
Fear of scarring at injecting site	75 (32.1)	159 (67.9)
Injecting insulin is embarrassing	68 (29.1)	166 (70.9)

Factors that may predict insulin treatment refusal were examined using simple logistic regression (Table III). Educational background and gender were found to be

Table III: Associated factors of insulin refusal by simple logistic regression analysis

Variable	Regression coefficient (b)	Crude OR (95%)	Wald statistic	p-value
Age (yr)	0.019	1.02 (0.99-1.05)	1.65	0.199
Duration since diagnosis (yr)	0.013	1.01 (0.96-1.07)	0.21	0.649
HbA1c (%)	0.010	1.01 (0.83-1.23)	0.01	0.919
Gender				
Male	0	1	4.27	0.039
Female	0.598	1.82 (1.03-3.21)		
Ethnicity				
Malay	0	1	0.332	0.564
Non-Malay	-0.172	0.84 (0.47-1.51)		
Employment Status				
Employed	0	1	0.47	0.495
Unemployed	-0.283	0.75 (0.33-1.70)		
Educational level				
Tertiary & Secondary	0	1	5.13	0.023
Primary & no formal	0.679	1.97 (1.10-3.55)		
Monthly income				
≤RM2000	0	1	0.77	0.380
>RM2000	0.264	1.30 (0.72-2.35)		

significantly associated with insulin treatment refusal. In terms of educational level, patients with no formal or only primary education were found to be 1.97 times more likely to refuse insulin therapy (crude OR 1.97, 95% CI 1.10-3.55, p=0.023). Female patients were 1.82 times more likely to refuse insulin therapy than male patients (crude OR 1.82, 95% CI 1.03-3.21, p=0.039).

We further examined the factors using multiple logistic regression analysis (Table IV). The results showed that patients with no formal or only primary education were 1.97 times more likely to refuse insulin therapy (adjusted OR 1.97, 95% CI 1.09-3.56, p=0.025), and female patients were 1.82 times more likely to refuse insulin therapy than male patients (adjusted OR 1.82, 95% CI 1.02-3.22, p=0.041). Educational background and gender were still significantly associated with reluctance to use insulin injections.

Table IV: Associated factors of insulin refusal by multiple logistic regression models

Variable	Regression coefficient (b)	Adjusted Odds Ratio (95%) ^a	Wald statistic	p-value
Educational level				
Tertiary & Secondary	0.677	1	5.04	0.025
Primary & no		1.97 (1.09-3.56)		
Gender				
Male	0.597	1	4.17	0.041
Female		1.82 (1.02-3.22)		

^a Forward LR Multiple Logistic Regression model was applied.

DISCUSSION

79.3% of the insulin-naïve T2DM patients in our setting refused insulin therapy. Most of our study population came from rural areas, and the result was consistent with the finding from Tan et al. 2015 (14). Another study done in urban areas in Malaysia (Kuala Lumpur and Putrajaya) showed a lower percentage (50.7%) of insulin therapy refusal (12). More patients from rural areas tend to refuse insulin therapy than those from urban areas, probably

due to inadequate diabetes education and insulin therapy misconception.

Various factors contribute to insulin treatment refusal among T2DM patients. This refusal of insulin therapy is often termed as 'psychological insulin resistance' or PIR (16). Based on our study, the most common factors contributing to insulin therapy refusal among T2DM patients were unconfident of injecting insulin (83.3%), failure of controlling diabetes mellitus (82.1%), and not showing any symptoms of poorly controlled diabetes mellitus. Less than a third expressed the reason being feeling embarrassed to inject insulin (29.1%).

Lack of confidence in injecting insulin among T2DM patients is common and a couple of studies showed that the injection-related issues are the primary factors contributing to insulin therapy refusal (13, 14). 85.4% of T2DM patients from rural areas in Malaysia refused insulin treatment because they were not confident to self-administer the insulin (14). Besides, a study conducted in Singapore also revealed that 70.6% of T2DM patients who refused insulin therapy did not feel confident in handling their daily insulin injection (13). The involvement of healthcare professionals during the initiation of insulin treatment can overcome the injection-related issues. Without proper explanation and demonstration from healthcare professionals, insulin therapy can be deemed as complicated and overwhelming. Some studies showed that demonstration of the insulin injection process was the most practical action to overcome PIR in T2DM patients (16, 17).

The second most common factor that contributing to insulin therapy refusal among T2DM patients in this study was patients' perception of the diabetes mellitus severity. They perceived that initiation of insulin therapy indicates that their condition has worsened and blamed themselves for needing insulin (12, 18). As suggested by Polonsky et al., an early explanation by the healthcare professions that insulin is necessary for glycaemic control in T2DM patients can reduce the earlier mentioned false perception (18).

In our study, educational background and gender were significantly associated with reluctance to use insulin. Female patients were 1.82 times more likely than male patients to reject insulin treatment. This finding was similar to Nur Azmiah et al., where female patients were 2.7 times more likely than male patients to refuse insulin treatment (12). According to Soylyar et al., females have a higher frequency of feeling fear of injection and greater social stigmatisation than males (19). These may be the possible explanations for the reason female patients were more likely to refuse insulin treatment.

Nonetheless, Tan et al. did not find any association between gender and insulin refusal (14), although the study setting was similar to our study. We cannot

deduce any reasonable explanation for the contrasting results. However, compared to Tan et al., our study and Nur Azmiah et al. (albeit in a different setting) had fewer female respondents (70.3% vs 57.6% and 42.8%, respectively, of total respondents). Further research has to be done to confirm whether this fact has any bearing on the results.

The possible factor contributing to insulin therapy refusal among T2DM patients with lower education in this study could be the poor understanding of the disease and the benefit of starting insulin treatment. Several studies showed similar findings in terms of education level, where a lower level of education was associated with a higher percentage of unwillingness to use insulin (13, 14). However, there was an intriguing finding from Puvanese et al. where they found that patients with higher education backgrounds have a higher frequency to refuse insulin therapy. Simultaneously, they noted that patients with poor insulin knowledge tend to refuse insulin treatment six times more than patients with better knowledge of insulin (20). These findings showed that having a higher educational level in some circumstances does not necessarily warrant a better understanding of insulin and its benefits.

The limitation this study is that our study did not examine healthcare providers' barriers, such as lack of experience, knowledge, and language barriers between healthcare providers and patients. Patients' knowledge level on diabetes mellitus was not assessed either.

CONCLUSION

The prevalence of insulin refusal is high in public health clinics in Segamat. Besides counselling, intervention steps should be taken to improve insulin acceptance by targeting the most typical reasons for insulin refusal in our setting: unconfident of injecting insulin and feeling of failure to control diabetes mellitus. Other factors, especially educational level and gender, should also be considered to address this problem. Future studies may focus on finding suitable approaches to reduce insulin therapy refusal among T2DM patients.

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REFERENCES

1. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 2014;31(Supplement 1):S81-90.
2. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances

- in the treatment and prevention. *International Journal of Medical Sciences*. 2014;11(11): 1185–1200.
3. Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes Burden in the United States, 2014. Atlanta, GA: U.S. Department of Health and Human Services; 2014.
 4. Institute for Public Health, Ministry of Health Malaysia. National Health and Morbidity Survey 2015 Vol. II: Non-Communicable Diseases, Risk Factors & Other Health Problems. Kuala Lumpur: Institute for Public Health; 2015.
 5. Institute for Public Health, Ministry of Health Malaysia. National Health and Morbidity Survey (NHMS) 2019: Vol. I: NCDs- Non-Communicable Diseases: Risk Factors and other Health Problems. Selangor: Institute for Public Health; 2020.
 6. Ministry of Health Malaysia. National Diabetes Registry Report 2013-2019. Putrajaya: Ministry of Health Malaysia; 2020.
 7. Chen Y-Y, Lin Y-J, Chong E, Chen P-C, Chao T-F, Chen S-A, et al. The Impact of Diabetes Mellitus and Corresponding HbA1c Levels on the Future Risks of Cardiovascular Disease and Mortality: A Representative Cohort Study in Taiwan. *PLoS ONE*. 2015;10(4): e0123116. doi:10.1371/journal.pone.0123116.
 8. Ministry of Health Malaysia. Clinical Practice Guidelines: Management of Type 2 Diabetes Mellitus. Putrajaya: Ministry of Health Malaysia; 2015.
 9. Turchin A, Hosomura N, Zhang H, Malmasi S & Shubina. Predictors and consequences of declining insulin therapy by individuals with type 2 diabetes. *Diabet Med*. 2020;37(5):814-21.
 10. Chen P, Ma X, Chen H, Wang K, Zhou L. Delays in insulin initiation among patients with type 2 diabetes mellitus in Southeast China: a retrospective, real-world study. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*. 2020;13:3059-68.
 11. Hosomura N, Malmasi S, Timerman D, Lei VJ, Zhang H, Chang L, et al. Decline of insulin therapy and delays in insulin initiation in people with uncontrolled diabetes mellitus. *Diabet Med*. 2017;34(11):1599-602.
 12. Nur Azmiah Z, Zulkarnain AK, Tahir A. Psychological insulin resistance among type II diabetes mellitus patients at public health clinic in Federal Territory of Malaysia. *International Medical Journal Malaysia*. 2011;10(2):7-12.
 13. Wong S, Lee J, Kot Y, Chong MF, Lam CK, Tang WE. Perceptions of insulin therapy amongst Asian patients with diabetes in Singapore. *Diabetes Medicine*. 2011;28:206-11.
 14. Tan WL, Asahar SF, Harun NL. Insulin therapy refusal among type II diabetes mellitus patients in Kubang Pasu district, Kedah, Malaysia. *Singapore Medical Journal*. 2015;56(4):224-7.
 15. Bahrmann A, Abel A, Zeyfang A, Petrak F, Kubiak T, Hummel J, Bahrmann P. Psychological insulin resistance in geriatric patients with diabetes mellitus. *Patient Education and Counseling*. 2014;94(3):417-22.
 16. Balogh EG, Perez-Nieves M, Cao D, Hadjiyianni II, Ashraf N, et al. Key strategies for overcoming psychological insulin resistance in adults with type 2 diabetes: the UK subgroup in the EMOTION Study. *Diabetes Ther*. 2020;11:1735-44.
 17. Okazaki K, Shingaki T, Cai Z, Perez-Nieves M, Lawrence F. Successful Healthcare Provider Strategies to Overcome Psychological Insulin Resistance in Japanese Patients with Type 2 Diabetes. *Diabetes Therapy*. 2019;10(5):1823-34.
 18. Polonsky WH, Arsenault J, Fisher L, Kushner P, Miller EM et al. Initiating insulin: how to help people with type 2 diabetes start and continue insulin successfully. *Int J Clin Pract*. 2017;71:8.
 19. Soyler P, Kadioglu BU, Kilic K. Investigation of the Barriers about insulin therapy in patients with type 2 diabetes. *Nigerian Journal of Clinical Practice*. 2020;23:98-102.
 20. Puvanese Rebecca PS, Salmiah MS, Ahmad ZF, Shamsul AS. Risk factors of insulin refusal among type 2 diabetes mellitus patients with poor glycaemic control at Tanglin Health Clinic, Kuala Lumpur. *Mal J Med Health Sci*. 2019;15(2):84-92.