Original Article

Hesitancy of Influenza Vaccination in Thai Patients with Type 2 Diabetes Mellitus: A Cross-sectional Study in Burapha University Hospital, Chonburi, Thailand

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Abstract

Objective: Despite influenza vaccines being recommended to patients with type 2 diabetes (T2DM), the coverage was still low. This study measured influenza vaccine hesitancy and identify associated factors among T2DM patients at the Burapha University Hospital.

Methods: This cross-sectional study was conducted during May-August 2020. Participants were recruited from T2DM patients visited the hospital for continuity care. The research gathered demographic data; medical data were retrieved from electronic medical records. Statistical analysis was performed for those who received the influenza vaccine compared to those who decided not to receive the vaccine.

Results: A total of 304 T2DM patients (female 54%, mean age 63 years, BMI 26.49kg/m^2, HbA1c 7.63%) were included into the study. One-third (30.6%) never had the vaccine. The hesitancy rate was 38%. When adjusted for demographic and medical data, T2DM patients aged < 65 years and never had influenza vaccines were significantly associated with the hesitancy. The top reason overall was lack of knowledge and awareness. Many patients did not have influenza vaccination because they had never received a vaccine recommendation from a primary provider.

Conclusions: Hesitancy to influenza vaccination was substantial among our T2DM patients especially those who were younger and never had the vaccine. Primary providers have a major role to raise the knowledge and awareness of influenza vaccine toward this vulnerable population.

Keywords: Influenza vaccination, Type 2 Diabetes Mellitus, Vaccine hesitancy

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Background

Influenza is a global health burden among general population and the severity is increasing among adults with chronic medical conditions including diabetes. A study in US found a 3.56 times higher risk for influenza and pneumonia mortality in patients with type 2 diabetes mellitus (T2DM).[1] In Thailand, diabetes patients' mortality of 0.4 per 100,000 per year was attributed to influenza; it was responsible for 3.8% of deaths in this patient group.[2] Therefore, influenza vaccine was recommended in patient with T2DM in order to prevent the infection and its consequences. Moreover, as the world is facing coronavirus disease 2019 (COVID-19) pandemic, diabetes patient is one of a risk groups prioritized by World Health Organization to receive influenza vaccine, considering that COVID-19 and influenza can co-circulate and put additional burden to entire health care system.[3]

Despite worldwide recommendations, influenza vaccine coverage was still low among diabetes patients. The studies during 2011-2013 found coverage rate ranged from 62% in South Korea, 52% in US, and 35% in Taiwan.[4, 5, 6] These figure has not yet matched with The World Health Organization (WHO) recommendation of 75% for diabetes patients.[7] Thailand Influenza vaccine usage among patient with chronic diseases was 10 - 13% during 2010 - 2012.[8] Data from National Health Security Office (NHSO) reported that in 2019 they supported influenza vaccine to 30.76% of population at risk (3,500,000 doses), and only 64.39% of the risk group actually received the vaccine, 35.41% of recipient were patient with chronic medical condition (716,613 patients).[9] This might not represent national vaccination rate as not all patients are under NHSO health scheme; however, one can assume that influenza coverage could be low considering there are at least 4.4 million T2DM patients in Thailand. The specific coverage data among diabetes patients was scarce and varied. The vaccination rate from a tertiary diabetes center in 2018 was 52%,[10] while the studies from local hospitals during 2016 - 2019 reported 68 - 89%.[11, 12]

Vaccine hesitancy was defined by the World Health Organization (WHO) as "delay in acceptance or refusal of vaccination despite availability of vaccine service".[13] It is considered to be one of the top ten public health threats. There was an inadequate assessment on factor contributed to vaccine hesitancy, especially among Asia Pacific regions. Local studies in Thailand reported association between influenza knowledge and vaccination rate in T2DM patients.[11, 12] Another study found a lower vaccination rate associated with younger age, shorter duration of diabetes diagnosis and less comorbidities.[10] However, the root cause of vaccine hesitancy among T2DM patients has yet to be explored. We need a clear perspective in order to effectively provide influenza vaccine to them. Therefore, our study measured the influenza vaccine coverage and determine the reason for vaccine hesitancy among adult T2DM patients at the internal medicine clinic, Burapha University Hospital.

Method

Overall study design and participants

We conducted a cross-sectional study among T2DM patients who visited internal medicine clinic at Burapha University Hospital, Chonburi, Thailand during May - August 2020. Monthly, the clinic receives an average of 350 T2DM patients but the number of patients during study period was decreased due to COVID pandemic. Upon clinic visit, the nurse will measure routine vital sign including BMI, and does the blood test per standard diabetic care. Then the patient is sent to the doctor for provision of treatment and prescription. During the visit, the doctor will decide to prescribe the influenza and other vaccines according to the standard practice. Patients are free to choose whether to receive the vaccine or not. Convenience sampling and recruitment were conducted by research staff after the clinical process. Inclusion criteria were patients aged 18 years or older with type 2 diabetes mellitus. Exclusion criteria were patients who had received previous influenza vaccine at other hospitals. Eligible patients were invited to read an information sheet followed by a written informed consent. After consented, participants were given paper questionnaire to answer. This research study was done at the end of all clinical process; the researchers did not intervene with any treatment/vaccination procedure. The average time to complete the questionnaire was less than 15 minutes.

Data measurement

Participants were asked to fill their demographic, age, gender, income, and education attainment. Medical and vaccination history were reviewed in electronic medical records and filled in by research staff. The medical history consisted of latest weight, body mass index (BMI), fasting blood sugar (FBS), HbA1c, creatinine, and calculated glomerular filtration rate (GFR). The vaccination history consisted of influenza and pneumococcal vaccination's date. Research staff also retrieved data regarding vaccines that patients were recommended and received on the current visit.

The additional part of questionnaire was for participants who chose not to receive an influenza vaccine per recommendation. They were asked the reasons behind vaccine hesitancy. The questionnaire has 3 main categories: contextual influences, individual influences, and vaccine/vaccination-specific issues. Each category comprises of 3 questions (total 9 items as in Table 3). Participant rated each of the items as least agree to most agree (scored 1-5). The questionnaire was adapted WHO SAGE model of determination of vaccine hesitancy into Thai context.[13] Validity testing was conducted using an expert panel comprising public health, family medicine, and internal medicine specialist. They rated items for content validity (-1 = not at all relevant to +1 = very relevant). Item Objective Congruence Index (IOC) was calculated from these ratings. The items that had scores lower than 0.5 were revised. On the other hand, the items that had scores higher than or equal to 0.5 were reserved. The final version of questionnaire was tested with 30 T2DM patients that were not in the sample group. Cronbach's alphas of 0.77 indicated that the responses to items were acceptably correlated.

Statistical analysis

The sample size was determined using the estimated proportion of vaccine hesitancy among T2DM patients in Thai hospital setting. There were 4.4 million patients with T2DM in Thailand. Recent studies reported the annual influenza vaccine coverage was 52%.[10, 11] While influenza vaccination history among T2DM patients at local hospitals reported to be 68-89%.[11, 12] The number was converted to an average of 22% vaccine hesitancy rate. Utilizing those data with an additional 15% to ensure the response rate, we estimated 304 T2DM patients needed to determine the associated factors for vaccine hesitancy with 95% confidence. The sample size calculation was performed with OpenEpi (Version 3.01, updated 2013/04/06).

Demographics, medical, and vaccination data were described for the participant cohort of T2DM patients. They were further classified by vaccine acceptance or hesitancy. The acceptance group consisted of patients who had received the influenza vaccine either within one year or at current visit per recommendation. The hesitancy group included those patients who choose not to receive the vaccine as recommendation. Categorical covariates were described as a number and percentage; continuous covariates were described as mean and Standard deviation (SD). Reason for vaccine hesitancy was presented by mean score. Comparisons between categorical and continuous variables in vaccine acceptance and hesitancy groups were made using Chi square. All *P*-values reported are two-sided, and statistical significance was defined as $P < 0.05$. Logistic regression was used to determine an odds ratio (OR) and 95 % confidence intervals (CI) for factors associated with being vaccine hesitancy. Multivariable models were developed adjusting for covariates in univariate models. We used Stata software version 12.1 (Stata Corp., College Station, TX, USA) for analysis. Study procedure were approved by the Burapha University Institutional Review Board.

Result

Baseline characteristic of the study population

From May to August 2020, 506 patients with T2DM visited the internal medicine clinic at Burapha University Hospital. We excluded 126 patients because they had received influenza vaccine at other hospitals. 304 (80%) were consent to participate in the study. Patients who did not consent mainly because they were in rush or did not want to spend more time in the hospital regarding COVID pandemic. Among 304 patients, 116 (38%) were already received influenza vaccine within one year. There were 95 patients who received influenza more than one year and 93 patients who never receive the vaccine; they were all recommended for influenza vaccine and 72 patients choose not to receive the vaccine (hesitancy rate 38%) (Figure 1).

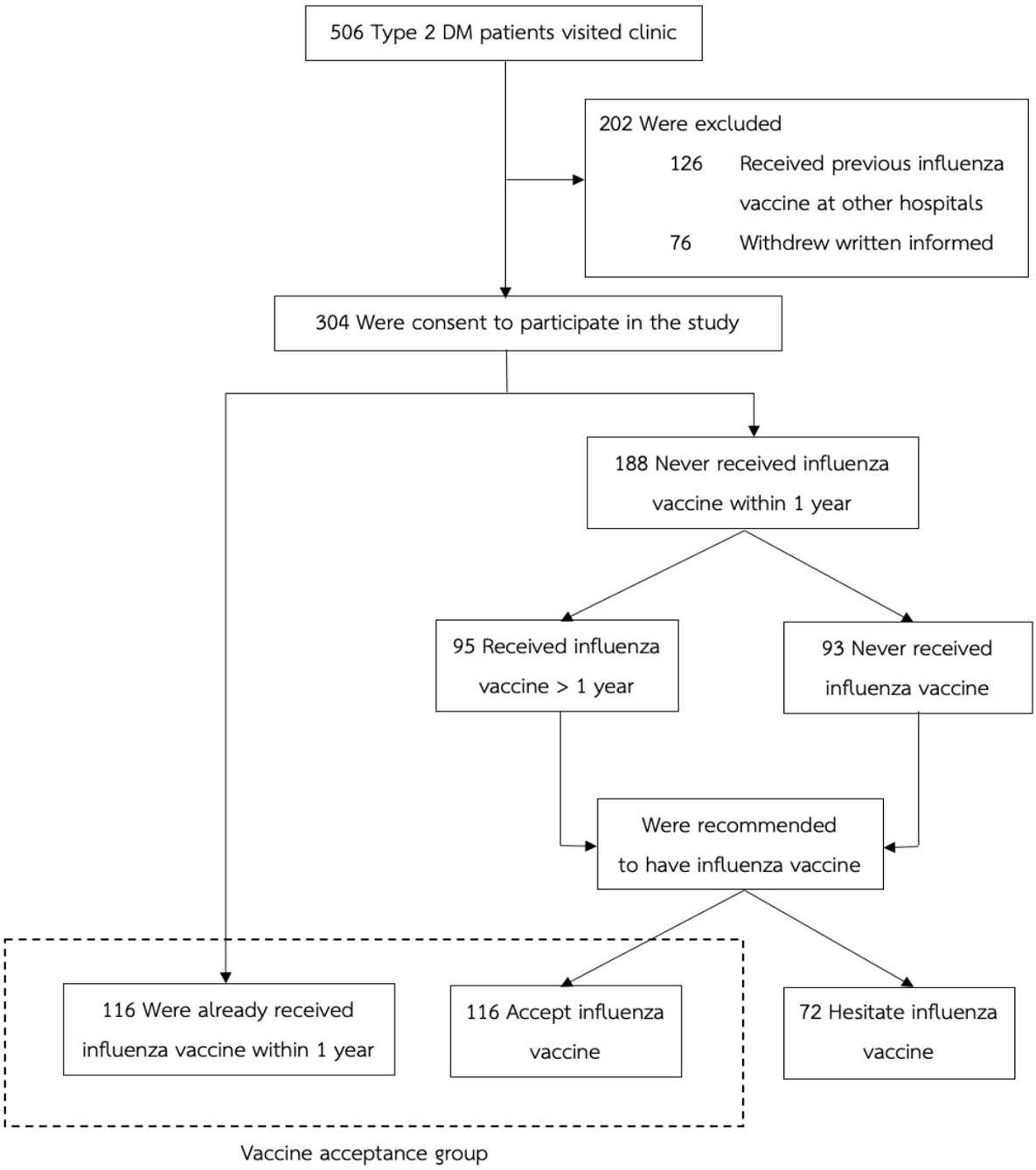

Figure 1 Flow diagram for study participants, Burapha University Hospital, Thailand 2020.

A total of 304 T2DM patients (232 vaccine acceptance and 72 vaccine hesitancy) were included in this analysis. More than half (54%) were female, with mean age of 63 (SD 13.53) years, mean BMI was 26.49 kg/m^2, and mean HbA1c was 7.63 %; one-third (30.6%) never received influenza vaccine before in life. 166 patients choose to receive vaccine at this this visit. The current influenza vaccine hesitancy rate was 38%. General demographic and medical data, classified by influenza vaccine acceptance status are presented in Table 1. Compared with patients who received influenza vaccine, vaccine hesitancy group were younger (mean age 64 years in vaccine acceptance and 59 years in hesitancy group, P 0.002), and higher in proportion of those who never had influenza vaccine (21% of vaccine acceptance and 61% of hesitancy group, $P < 0.001$).

Table 1 Demographic of patients with type 2 diabetes (T2DM) (N = 304) who visited Burapha University Hospital, classified by vaccine acceptance status

	Total (N = 304) N (%)	**Accept Flu vaccine (N = 232) N (%)**	**Hesitancy (N = 72) N (%)**	***P*-value**
General demographic				
- Age, year mean (SD)	63 (13.53)	64 (13.47)	59 (12.84)	0.002*
- Female	165 (54.28%)	129 (55.6%)	36 (50%)	0.645
- Male	139 (45.72%)	103 (44.4%)	36 (50%)	
- Education				
Primary school	13 (4.3%)	9 (3.9%)	4 (5.6%)	
Secondary school	118 (38.8%)	92 (39.7%)	26 (36.1%)	
Junior high school	21 (6.9%)	14 (6%)	7 (9.7%)	
Senior high school	48 (15.8%)	39 (16.8%)	9 (12.5%)	
High Vocational Certificate	14 (4.6%)	10 (4.3%)	4 (5.6%)	
≥ Bachelor's degree	90 (29.6%)	68 (29.3%)	22 (30.6%)	
- Monthly income, Baht				
0 - 9,999	151 (49.7%)	123 (53.0%)	28 (38.9%)	
10,000 - 25,000	84 (27.6%)	56 (24.1%)	28 (38.9%)	
25,001 - 50,000	50 (16.4%)	39 (16.8%)	11 (15.3%)	
> 50,001	19 (6.3%)	14 (6%)	5 (6.9%)	
Medical data				
- Body weight (kg), mean (SD)	69.08 (15.05)	68.42 (14.7)	71.22 (16.07)	0.262
- BMI (kg/m^2), mean (SD)	26.49 (5.12)	26.35 (5.21)	26.95 (4.81)	0.414
- FBS (mg/dL), mean (SD)	154.05 (67.66)	151.39 (66.64)	165 (70.45)	0.153
- HbA1c (%), mean (SD)	7.63 (1.63)	7.57 (1.57)	7.81 (1.77)	0.165
- GFR(mL/min/1.73m^2), mean (SD)	81.30 (65.57)	80.70 (77.17)	82.19 (43.26)	0.397
- Never received Flu vaccine	93 (30.6%)	49 (21.1%)	44 (61.11%)	< 0.001*

BMI: body mass index, FBS: fasting blood sugar, GFR: glomerular filtration rate

Factors associated with vaccine hesitancy

In univariate analysis, Table 2, the following factors were significantly associated with being vaccine hesitancy: (1) age < 65 years, (2) never received influenza vaccine. When adjusted for demographics and medical data, T2DM patient aged < 65 years (aOR 2.52 (95 %CI 1.00 - 6.35), *P* = 0.049) and never received influenza vaccine (aOR 3.08 (95 %CI 1.27 - 4.267.46), *P* = 0.013) were independently associated with influenza vaccine hesitancy.

Table 2 Univariate and multivariate association of influenza vaccine hesitancy among T2DM patients who visited Burapha University Hospital

Independent variable	Univariate			Multivariate		
	OR	95% CI	*P*-value	aOR	95% CI	*P*-value
General demographic						
- Age < 65 years	2.88	1.63 - 5.10	< 0.001*	2.52	1.00 - 6.35	0.049*
- Monthly income < 10,000 baht	0.56	0.33 - 0.97	0.036*	0.40	0.16 - 1.00	0.050
Medical data						
- Obesity (BMI ≥ 35 or BW ≥ 100 kg)	1.99	0.84 - 4.72	0.114			
- HbA1C > 6.5%	1.13	0.59 - 2.15	0.713			
- GFR < 60 mL/min/1.73m^2	0.77	0.36 - 1.67	0.514	3.08	1.27 - 7.46	0.013*
- Never received Flu vaccine	5.87	3.32 - 10.37	< 0.001*			

GFR: glomerular filtration rate

Reasons for vaccine hesitancy

Results of the reasons for vaccine hesitancy are summarized by mean scores in Table 3. Overall, the main reasons were the influence from both individual and contextual. Reasons ranked from highest were "not received enough information of vaccine", "The vaccine was not promoted by the media", "Perceived the disease to be low risk", and "the vaccine did not regard as national policy". The pattern of main reasons for vaccine hesitancy were same when we sub-grouped T2DM patients who aged < 65 year. However, for those who have never received influenza vaccine, "never received vaccine recommendation from primary provider" emerged to be a main reason. Cost of vaccine, hospital vaccination process, and personal experience of vaccine adverse event were three lowest reasons for vaccine hesitancy.

Table 3 Reason for influenza vaccine hesitancy among T2DM patients who visited Burapha University Hospital, presented by mean score

Question	Age (years)		Income (THB)		Receive Flu vaccination	
	< 65	≥ 65	< 10,000	≥ 10,000	Ever	Never
-The vaccine was not promoted by the media	3	3	3	3	3	3
-The vaccine did not regard as national policy	3	3	3	2	3	2
-Hospital vaccination process	2	2	2	2	2	2
-Not received enough knowledge of vaccine	3	3	3	3	3	3
-Perceived the disease to be low risk	3	3	3	3	3	3
-Personal experience of vaccine adverse event	2	2	2	2	2	2
-Cost of vaccine	2	2	2	2	2	2
-Vaccine safety concern	2	2	3	2	2	2
-Never received vaccine recommendation from primary provider	2	2	2	2	2	3
sum	22	22	23	21	22	22

Discussion

In this study, we reported 38% influenza vaccine hesitancy rate among a sample of T2DM patients who were followed up at the internal medicine clinic, Burapha University Hospital, Chonburi, Thailand. The overall vaccine coverage among these patients was 76%; the number was comparable to WHO recommendation of 75% and higher than previous studies in Thailand. This may explain by that this research was done during COVID pandemic. There was a substantial group of patients who were keen for preventive measures, including influenza vaccine. The vaccine was also recommended by many health organizations both locally and internationally.[3] The doctor awareness of influenza vaccine thereby increased. Despite the situation, influenza vaccine hesitancy in our cohort was still worrisome. In fact, the vaccination rate was expected to be much higher in our cohort considering that their blood sugar was primarily uncontrolled (mean HbA1c 7.63%, mean FBS 154 mg/dL). Influenza infection could be more severe through direct immunosuppression effect of glucose and increasing risk of secondary bacterial infections.[14]

We found that those aged < 65 years and never received influenza vaccine were significantly associated with influenza vaccine hesitancy. The finding was in line with a Thai study in 2018 that the strong predictive factors for T2DM patients to receive influenza vaccination were age ≥ 65 years and the presence of co-morbidities such as chronic pulmonary diseases. In contrast, diabetic factors alone may have been ignored as indication for influenza vaccine.[10] Moreover, patient with poorer glycemic control may represent lower self-care and lower adherence to medication and preventive measures. A Spanish cohort identified T2DM patients with higher mean HbA1C was associated with a reduced probability of vaccination.[15] Those who never received the vaccine tended to be hesitate in vaccine. In a cohort of Thai older adult, history of receiving vaccination was found to be associated with influenza vaccine acceptance.[16]

The top reasons for vaccine hesitancy among our patients included “not received enough knowledge of vaccine”, “The vaccine was not promoted by the media”, and “Perceived the disease to be low risk”. The reason was supported by a cohort of Thai older adults, the study found an acceptance of influenza vaccine increased along with increase in knowledge after an educational video.[16] The WHO surveyed on vaccine hesitancy During 2014 - 2016; they identified “vaccine safety concerns”, “knowledge and awareness” and “design of vaccination process” to be main reasons for hesitancy reasons in South East Asian region. The first and third reason were ranked lower in our study. However, the author on WHO paper discussed that majority of hesitancy reasons in that survey were not based on assessment but on opinion. There may be different in reasons between formal assessment and opinion-based.[17] The difference could be varied among individual context and vaccine as well. We found that among T2DM patients who have never received influenza vaccine, “never received vaccine recommendation from primary provider” emerged to be within top reasons.

There are some limitations in our study. First, the reasons and factors associated with influenza vaccine hesitancy could not be generalized to different vaccines and context. For examples, only 3% of T2DM patients in our study choose to receive pneumococcal vaccine (data not shown) despite being recommended by the doctor. Cost may be a primary reason here; we plan to explore further in the following study. Second, this study used convenience sampling and a cross-sectional study design, which prevents us from making causal inference between variables and vaccine hesitancy. Third self-reported vaccine history can be incorrect. However, we verified the vaccine history with electronic medical record for every included participant. Lastly, patients and providers may be more aware of influenza vaccine promoted during COVID pandemics, the findings must be interpreted in light of the situation.

This study utilized WHO vaccine hesitancy framework and applied toward influenza vaccine service in specialized DM clinic in Thailand. We suggested substantial vaccine hesitancy despite being a higher risk group for influenza complication. There were two subgroups that should receive special attention. First, T2DM patients aged younger than 65 years. They might not be aware that being T2DM alone put them in a risk group, and influenza vaccine for the group was promoted as national public health policy since 2009. Moreover, younger patients could potentially transmit the virus onward.

The second group was patients who never receives influenza vaccine before. Previous study suggested more proportion of vaccine acceptance in those with history of receiving vaccination.[16] Primary doctor should play a significant role in vaccine education. The data among cardiovascular patients in Chiang Mai described the main reason of missing influenza vaccine to be "patient was not encouraged and motivated to be vaccinate".[18] While individual patient requires more awareness on the vaccine from their providers, media and policy maker could help to reach out and spread the information.

In summary, influenza vaccine hesitancy is still substantial among T2DM patients at Burapha University Hospital. Vaccine hesitancy is associated with patients younger than 65 years and those who have never received the vaccine. Influenza viruses continuously change and wide-spread. In order to prevent serious complication and transmission, health care providers, media and policy makers should work together to raise the knowledge and awareness among this vulnerable group.

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