Contents lists available at IOCS

Science Midwifery

journal homepage: www.midwifery.iocspublisher.org

The relationship between knowledge and adherence to insulin therapy in type 2 diabetes mellitus patients at the outpatient clinic of Budi Kemuliaan Hospital, Batam City

Aprilya Sri Rachmayanti[1], Nahrul Hasan[2], Suci Fitriani Sammulia[3], Reny Haryani[4], Suhaera[5], Rastria Meilanda[6], Asmina Sinaga[7]

[1,2,3,4]Program Studi Pendidikan Profesi Apoteker, Institut Kesehatan Mitra Bunda, Batam, Indonesia
[5,6,7]Program Studi Sarjana Farmasi, Institut Kesehatan Mitra Bunda, Batam, Indonesia

ARTICLE INFO

Article history:

Received Nov 30, 2023
Revised Dec 2, 2023
Accepted Dec 11, 2023

Keywords:

Adherence
Insulin Therapy
Knowledge
Type 2 Diabetes Mellitus

ABSTRACT

Diabetes mellitus is a prevalent degenerative disease in today's society. Indonesia, as one of the countries with the largest population, has experienced a significant increase in the global prevalence of type 2 diabetes mellitus. Approximately 20% of the Indonesian population uses insulin with or without oral antidiabetic drugs. It has been found that patient compliance in Indonesia does not meet the recommended glycemic targets. This non-compliance is attributed to patients' lack of knowledge and understanding about insulin and its use in therapy. This study aims to explore the relationship between knowledge and adherence to insulin therapy among type 2 diabetes mellitus patients in the outpatient clinic of Budi Kemuliaan Hospital, Batam City. A descriptive correlation method was employed, utilizing a prospective cross-sectional research design. The sample was selected using purposive sampling, resulting in a total of 60 patients who met the inclusion criteria. Data were collected through two questionnaires: a knowledge questionnaire and the Medication Adherence Scale (MMAS). Statistical analysis included frequency distribution tests and chi-square tests. The research findings revealed a significant relationship between knowledge and adherence to insulin therapy, with a Chi-Square test yielding a P-Value of 0.029, where P-Value $\alpha < 0.05$. In conclusion, this study demonstrates a significant correlation between knowledge and adherence to insulin therapy among type 2 diabetes mellitus patients. It is recommended that healthcare providers at Budi Kemuliaan Hospital deliver accurate information to patients to enhance their knowledge and understanding of insulin use, as well as the potential complications associated with diabetes mellitus.

Corresponding Author:

Nahrul Hasan,
Program Studi Pendidikan Profesi Apoteker,
Institut Kesehatan Mitra Bunda,
Jl. Raya Seraya Nomor No.1, Tlk. Tering, Kec. Batam Kota, Kota Batam, Kepulauan Riau 29444, Indonesia,
Email: nahrulhasan@gmail.com

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels and alterations in fat and protein metabolism due to defects in insulin secretion, insulin action, or both (Lestari & Amir, 2019). The prevalence of type 2 diabetes mellitus is increasing in various countries, including Indonesia, and treatment adherence to diabetes is varied in developing countries (Al-Lela et al., 2020; Sahoo et al., 2022). In Indonesia, there has been an increase in the prevalence of diabetes mellitus, including in the Riau Islands, and patient adherence to treatment remains low (Dinas Kesehatan Kota Batam, 2018; Kementerian Kesehatan, 2018).

Patient adherence to insulin therapy poses a challenge that can affect treatment outcomes (Duru et al., 2010; Inamdar et al., 2013). Factors influencing non-adherence include demographic factors, understanding of the disease, patient-healthcare provider relationships, psychological factors, health knowledge, and social factors. Non-adherence to insulin therapy can lead to treatment failure and an increased risk of complications (American Diabetes Association, 2015).

Patient knowledge about insulin therapy is crucial for the success of type 2 diabetes mellitus treatment (Priscilla et al., 2019). However, inadequate patient knowledge regarding insulin usage can result in incorrect dosing, improper injection timing, and the risk of hypoglycemia (Alfian, 2016). Several studies have shown that the level of patient knowledge does not always correlate with the level of adherence to insulin therapy (Alfian, 2016; Sartunus et al., 2015).

Non-adherence to insulin therapy by patients can lead to serious microvascular and macrovascular complications (American Diabetes Association, 2015). It is important for healthcare professionals to provide accurate and comprehensive information to patients regarding insulin usage and ensure that patients understand and adhere to their therapy (Ejeta et al., 2015). Based on the aforementioned background, the researchers aim to investigate the relationship between knowledge and adherence to insulin therapy among Type 2 diabetes mellitus patients at the Outpatient Clinic of Budi Kemuliaan Hospital in Batam City. This research seeks to deepen our understanding of the factors influencing adherence to insulin therapy, ultimately aiming to improve treatment outcomes and enhance the overall quality of diabetes care at Budi Kemuliaan Hospital in Batam City.

RESEARCH METHOD

This study is a correlational descriptive research aimed to examine the relationship between knowledge and adherence to insulin therapy in patients with Type 2 Diabetes Mellitus. The study employed a prospective cross-sectional design, where data was collected at a single point in time and each research subject was observed only once. The study population consisted of 155 patients receiving insulin therapy as outpatient at Budi Kemuliaan Hospital Batam. The research sample comprised all Type 2 Diabetes Mellitus patients who met the inclusion and exclusion criteria, using purposive sampling technique to select samples representing the population characteristics. The inclusion criteria included patients diagnosed with Type 2 diabetes mellitus, using insulin therapy, and willing to participate in the study with a minimum age of 15 years. The exclusion criteria included children and pregnant women. The sample size was calculated using the formula by Lemeshow et al., and based on the calculation results, the minimum sample size was determined as 60 respondents.

The study was conducted in the outpatient department of Budi Kemuliaan Hospital Batam in August 2021. The research variables consisted of an independent variable, which was the knowledge of insulin therapy in patients with Type 2 diabetes mellitus, and a dependent variable, which was the adherence to insulin therapy in patients with Type 2 diabetes mellitus. Data was collected through interviews using a questionnaire as the data collection tool. The questionnaire comprised two types: the Morisky's Medication Adherence Scale (MMAS-8) questionnaire with 8

questions, and the questionnaire on knowledge about insulin therapy with 18 questions. The questionnaires were tested for validity and reliability before being used. The research instruments used included medical records, prescriptions, the Morisky's Medication Adherence Scale (MMAS-8) questionnaire, and the questionnaire on knowledge about insulin therapy. Medical records were used to obtain patients' medical data, while prescriptions were used to record information related to prescribed insulin therapy. The MMAS-8 questionnaire was used to measure the level of adherence to insulin therapy in patients, while the questionnaire on knowledge about insulin therapy was used to measure the level of patients' knowledge about insulin therapy.

Data analysis was conducted using SPSS software. The validity of the instruments was tested using Pearson's Product Moment Correlation Bivariate by comparing the test results with correlation values in the correlation table. The reliability of the instruments was tested using Cronbach's alpha with a reliability criterion above 0,60.

The collected data was examined for completeness, and then analyzed descriptively using frequency distribution tables and percentages. Univariate analysis was used to describe the characteristics of the research variables, both independent and dependent variables. Bivariate analysis was used to evaluate the relationship between the knowledge of insulin therapy (independent variable) and adherence to insulin therapy (dependent variable).

Ethical aspects of the research were upheld in this study, including informed consent, anonymity, confidentiality, and fairness. Informed consent was obtained from participants, ensuring they received sufficient information about the study before giving consent. Participants' identities were kept anonymous using codes instead of names. Confidentiality of collected information was ensured, and only a specific group had access to the data for reporting purposes. The principle of fairness was upheld, treating all participants fairly and respecting their rights throughout the research.

RESULTS AND DISCUSSIONS

The study was conducted from August 1, 2021, to September 30, 2021, with the aim of evaluating the relationship between knowledge and adherence to insulin therapy in type 2 diabetes patients at the outpatient clinic of Budi Kemuliaan Hospital in Batam City. The study involved a total of 60 respondents. Collected patient characteristics data included age, gender, education level, occupation, health insurance, insulin and oral antidiabetic therapy, type of insulin used, and comorbidities.

Table 1. Frequency distribution of patient characteristics

Variable	Category	Frequency (n)	Percentage (%)
Age	15 - 25	0	0
	26 - 45	11	18.3
	46 - 65	39	65.0
	>65	10	16.7
	Total	60	100
Gender	Male	30	50.0
	Female	30	50.0
	Total	60	100
Education Level	Elementary School	8	13.3
	Junior High School	12	20.0
	Senior High School	29	48.3
	College/University	11	18.4
	Total	60	100
Occupation	Government employees	5	8.3
	Housewife	18	30.0
	Merchant	7	11.7
	Private Employee	21	35.0
	Retiree	9	15.0
	Total	60	100

Variable	Category	Frequency (n)	Percentage (%)
Health Insurance	Public	0	0
	Private	0	0
	BPJS	60	100
	Total	60	100

Patient characteristics (table 1) based on age showed that the majority of patients (65.0%) were in the age range of 46-65 years. This is consistent with previous research indicating an increased prevalence of diabetes and impaired glucose tolerance with advancing age (Sartunus et al., 2015). Patient characteristics based on gender indicate an equal distribution between females and males in this study, with 30 (50%) females and 30 (50%) males. Health behavior differences between males and females are explained by Darusman (2009), where generally women tend to pay more attention and care to their health and undergo treatment more frequently compared to men (Darusman, 2009). Patient characteristics based on educational level indicate that the dominant educational level is high school (SMA), with 29 patients (48.3%). This aligns with the statement by Siti (2019), asserting that educational level is one of the predisposing factors influencing individuals' utilization of healthcare services (Siti & Indrawati, 2019). Patient characteristics based on occupation indicate that the majority of patients work in the private sector, comprising 21 patients (35%). The findings of Fitrani et al (2019) suggest that being employed is often a time-consuming activity, which may hinder an individual's adherence to insulin usage (Fitriani et al., 2019). All 60 patients (100%) utilize BPJS insurance due to the ongoing and costly nature of type 2 diabetes mellitus therapy.

Table 2. Frequency distribution of patient characteristics based on insulin and oral antidiabetic therapy, the type of insulin used, and coexisting diseases

Variable	Category	Frequency (n)	Percentage (%)
Insulin and Oral Antidiabetic (OAD)	Single Insulin	10	16,67
	Single Insulin + OAD	35	58,33
	Insulin Combination	6	10
	Insulin Combination + OAD	9	15
	Total	60	100
Insulin Type	Ezelin	2	3.3
	Lantus	13	21.7
	Levemir	7	11.7
	Novomix	4	6.7
	Novorapid	10	16.7
	Novorapid & Ezelin	1	1.7
	Novorapid & Levemir	4	6.7
	Novorapid & Sansulin	10	16.7
	Sansulin	9	15.0
	Total	60	100
Comorbidities	Type 2 DM	9	15.0
	Type 2 DM , Hypertension	24	40.0
	Type 2 DM, Hypertension, Dyslipidemia	1	1.7
	Type 2 DM. Myalgia	2	3.3
	Type 2 DM, Anemia	1	1.7
	Type 2 DM, Neuropathy, CHF	2	3.3
	Type 2 DM, Hypertension, Neuropathy	3	5.0
	Type 2 DM, CAD	1	1.7
	Type 2 DM, Hypertension, Polyneuropathy	3	5.0
	Type 2 DM, Gangren	4	6.7
	Type 2 DM, Hypertension, ESRD	2	3.3
	Type 2 DM, Hypertension, Hep B	1	1.7
	Type 2 DM, Cardioemboli	1	1.7
	Type 2 DM, Hep B	2	3.3
	Type 2 DM, CHF	2	3.3
	Type 2 DM, B20	2	3.3

Variable	Category	Frequency (n)	Percentage (%)
	Total	60	100

Characteristics of patients based on insulin and oral antidiabetic therapy in table 2 reveal that the widely utilized treatment is insulin with metformin, involving 14 patients (23.3%). The combination of metformin and long-acting insulin (insulin glargine) effectively lowers fasting blood sugar levels to achieve the target. Combining oral antidiabetic drugs with basal insulin generally results in effective blood glucose control (PERKENI, 2015). Characteristics of patients based on the type of insulin used reveal that the most dominant insulin type is Lantus (Insulin Glargine), with 13 patients (21.7%). This preference stems from Lantus (Insulin Glargine) belonging to the basal insulin category, considered safe for combination with oral antidiabetic drugs to achieve glycemic reduction without the risk of hypoglycemia. Lantus has a duration of action of 12-24 hours and has nearly peakless effects (PERKENI, 2015). Characteristics of patients based on comorbidities indicate that the majority suffer from Type 2 Diabetes Mellitus along with hypertension, involving 24 patients (40.0%). Research shows that hypertension is most commonly found in patients with Type 2 DM due to elevated and uncontrolled blood glucose levels, leading to arterial narrowing, reduced elasticity, and arteriosclerosis. If not addressed, arteriosclerosis can trigger hypertension, heart damage, and kidney failure (Petrie et al., 2018).

Table 3. Frequency distribution of knowledge levels and adherence levels in Type 2 diabetes mellitus patients

Variable	Category	Frequency (n)	Percentage (%)	
Patient Knowledge	Good	43	71.7	
	Moderate	15	25.0	
	Poor	2	3.3	
	Total	60		100
Patient Compliance	High	10	16.7	
	Moderate	13	21.7	
	Low	37	61.6	
	Total	60		100

At Budi Kemuliaan Hospital, 71.7% of patients exhibit a strong understanding of insulin therapy (table 3), consistent with Handayani et al (2017) study on the relationship between knowledge and adherence to insulin use in diabetes patients (Handayani et al., 2017). Assessment of compliance questionnaire shown in table 4. Comprehensive knowledge significantly contributes to the success of diabetes therapy, influencing better outcomes. Patients receiving both oral antidiabetic and insulin therapy must have essential knowledge about insulin's purpose and proper administration to avoid hindering the therapeutic process and potential harm. Incorrect insulin dosages, whether excessive or insufficient, pose risks, leading to dangerous hypoglycemia or elevated blood sugar levels (Petersen & Shulman, 2018). Crucially, patients need awareness of the optimal timing for insulin administration—fifteen minutes before meals—to effectively reduce postprandial blood glucose levels. The overall conclusion is that Type 2 diabetes mellitus patients with good knowledge exhibit positive influences on their mindset and behavior, particularly in adhering to insulin therapy (Luijf et al., 2010; Slattery et al., 2018).

Adherence to insulin therapy at Budi Kemuliaan Hospital is notably low, with 61.6% of patients showing poor adherence. Non-adherence significantly contributes to diabetes mellitus therapy failure, risking uncontrolled blood glucose levels and organ damage (Davies et al., 2022). This lack of adherence is linked to patients' insufficient knowledge of insulin and its therapeutic use. Such non-adherence may result in treatment failure and toxicity (Piragine et al., 2023). The researcher attributes patient non-adherence to forgetfulness, the perception of insulin worsening their condition, lapses in carrying insulin while traveling, discontinuation when conditions improve, daily discomfort, and frequent challenges.

Table 4. Assessment of compliance questionnaire

No	Question	Yes	%	No	%
1.	Have you ever forgotten to use insulin?	31	51,70%	29	48,30%
2.	Besides forgetting, have there been days in the last 2 weeks when you did not use the medicine?	3	5%	57	95%
3.	Have you ever reduced or stopped using insulin without the doctor's knowledge because you felt that the insulin given made your condition worse?	15	25%	45	75%
4.	Have you ever forgotten to bring insulin when traveling?	20	33,30%	40	66,70%
5.	Did you use insulin yesterday?	38	63,30%	22	36,70%
6.	Have you stopped using insulin when you feel your condition is better?	13	21,70%	47	78,30%
7.	Using insulin every day may cause discomfort for some people. Do you feel bothered having to use insulin every day?	30	50%	30	50%
8.	How often do you have difficulty remembering to take medication?				
	a. Never				
	b. Occasionally				
	c. Sometimes	28	46,70%		
	d. Usually	32	53,30%		
	e. Always/Often				

The majority of type 2 diabetes mellitus patients, as per table 5, demonstrate low adherence to insulin therapy, with 61.6% (37 patients). Among those with good knowledge, 35% (21 patients) exhibit low adherence. A significant relationship is evidenced by the Chi-Square test, with a p-value of 0,029 (p-value $\alpha < 0.05$). Consequently, Ho is rejected, and Hα is accepted, leading to the conclusion that "There is a significant relationship between knowledge and adherence to insulin therapy," indicating that individual knowledge correlates with adherence. These findings are consistent with Marbun's (2021) research, showing a significant correlation between knowledge and adherence in Type 2 diabetes patients (Marbun, 2021).

Table 5. Analysis of the relationship between knowledge and adherence to insulin therapy

Knowledge	Adherence						Total		P- Value
	High		Moderate		Low				
	N	(%)	N	(%)	N	(%)	N	(%)	
Good	10	16,7	12	20	21	35	43	71,7	
Adequate	0	0	1	1,7	14	23,3	15	25,0	
Poor	0	0	0	0	2	3,3	2	3,3	0,029
Total	10	16,7	13	21,7	37	61,6	60	100	

The role of healthcare providers is crucial in influencing knowledge, positively impacting patient adherence to insulin therapy. Family support also plays a vital role as a close support system, motivating individuals undergoing therapy. Initial knowledge provided to diabetes mellitus patients encompasses the disease journey, control and monitoring, complications, pharmacological and non-pharmacological therapies, interactions, exercise, self-monitoring of blood glucose, managing hypoglycemia, the importance of exercise, foot care, and utilizing healthcare facilities. Studies suggest that a lack of knowledge about diabetes mellitus may lead patients to reject insulin (PERKENI, 2015; Tan et al., 2015) .

Table 6. The relationship between patient characteristics and adherence.

Characterisric	Adherence High N	Moderate N	Low N	Total N	P- Value
Gender					
Male	6	9	15	30	
Female	4	4	22	30	0,161
Total	10	13	37	60	
Age					
26 - 45	5	1	5	11	
46 - 65	5	10	24	39	
>65	0	2	8	10	0,048
Total	10	13	37	60	
Education Level					
Elementary School	0	1	7	8	
Junior High School	0	0	12	12	
Senior High School	4	7	18	29	
College/University	6	5	0	11	0,000
Total	10	13	37	60	
Occupation					
Government employees	5	0	0	5	
Housewife	1	3	14	18	
Merchant	0	1	6	7	
Private Employee	4	6	11	21	0,000
Retiree	0	3	6	9	
Total	10	13	37	60	

The researcher finds that age, education, occupation, and knowledge significantly influence patient adherence to insulin therapy (table 6). Aging factors in limitations to physiological functions, with older age associated with decreased cognitive functions. Education, facilitating behavioral changes and improved cognitive abilities, plays a significant role. Lower education levels are associated with lower adherence, highlighting that higher education positively impacts awareness and knowledge of insulin therapy. Occupation also correlates significantly with adherence, with housewives predominantly exhibiting low adherence. Age, education, occupation, and knowledge are influential factors in patient adherence to insulin therapy.

CONCLUSION

Budi Kemuliaan hospitals outpatient clinic involving 60 respondents reveals significant findings. While a substantial majority of Type 2 diabetes mellitus patients (71.7% or 43 individuals) demonstrate commendable knowledge, a contrasting trend emerges in terms of adherence to insulin therapy. A noteworthy majority, comprising 61.6% or 37 patients, exhibits low adherence to the prescribed insulin regimen. The key observation highlights a significant relationship between knowledge and adherence to insulin therapy among Type 2 diabetes mellitus patients at Budi Kemuliaan Hospital in Batam City. This suggests that patients with higher knowledge levels are more likely to adhere to their insulin therapy. In essence, while a significant portion of Type 2 diabetes mellitus patients demonstrates good knowledge, a notable proportion faces challenges in adhering to insulin therapy. The research is expected to serve as a valuable source of information for enhancing knowledge in health sciences, particularly regarding diabetes mellitus, and as a reference for providing better health services to achieve success in diabetes management. For future researchers, it is recommended to expand the scope by including a larger and more diverse sample, involving healthcare professionals and multiple hospitals.

ACKNOWLEDGEMENTS

Thank you to Budi Kemuliaan Hospital, Batam City who has permitted it to be used as a research location.

References

Alfian, R. (2016). Hubungan Antara Pengetahuan Dengan Kepatuhan Tentang Penggunaan Insulin Pada Pasien Diabetes Mellitus Di Poliklinik Penyakit Dalam Rsud. Dr. H. Moch. Ansari Saleh Banjarmasin. *Jurnal Ilmiah Ibnu Sina,1(1), 9-18, 2016*, *1*(1), 9–18.

Al-Lela, O. Q. B., Abdulkareem, R. A., AL-Mufti, L., Kamal, N., Qasim, S., Sagvan, R., Hinir, Z., & Khidr, H. (2020). Medication adherence among diabetic patients in developing countries: Review of studies. *Systematic Reviews in Pharmacy*, *11*(8), 270–275. https://doi.org/10.31838/srp.2020.8.39

American Diabetes Association. (2015). Standards of Medical Care in Diabetes—2015 Abridged for Primary Care Providers. *Clinical Diabetes*, *33*(2), 97–111. https://doi.org/10.2337/diaclin.33.2.97

Darusman. (2009). Perbedaan Perilaku Pasien Diabetes Mellitus Pria dan Wanita dalam Mematuhi Pelaksanaan Diet. In *Berita Kedokteran Masyarakat* (Vol. 25, Issue 1). http://www.stanforddaily.com/article/1999/

Davies, M. J., Aroda, V. R., Collins, B. S., Gabbay, R. A., Green, J., Maruthur, N. M., Rosas, S. E., Del Prato, S., Mathieu, C., Mingrone, G., Rossing, P., Tankova, T., Tsapas, A., & Buse, J. B. (2022). Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*, *45*(11), 2753–2786. https://doi.org/10.2337/dci22-0034

Dinas Kesehatan Kota Batam. (2018). *Profil Kesehatan Kota Batam Tahun 2018*.

Duru, O. K., Schmittdiel, J. A., Dyer, W. T., Parker, M. M., Uratsu, C. S., Chan, J., & Karter, A. J. (2010). Mail-order pharmacy use and adherence to diabetes-related medications. *The American Journal of Managed Care*, *16*(1), 33–40.

Ejeta, F., Raghavendra, Y., & Wolde-Marian, M. (2015). Patient Adherence to Insulin Therapy in Diabetes Type 1 and Type 2 in Chronic Ambulatory Clinic of Jimma University. *International Journal of Pharma Science and Research*, *6*(4), 796–806.

Fitriani, Y., Pristianty, L., & Hermansyah, A. (2019). Pendekatan Health Belief Model (HBM) untuk Menganalisis Kepatuhan Pasien Diabetes Melitus Tipe 2 dalam Menggunakan Insulin. *PHARMACY: Jurnal Farmasi Indonesia (Pharmaceutical Journal of Indonesia)*, *16*(2), 167. https://doi.org/10.30595/pharmacy.v16i2.5427

Handayani, Nuravianda, Y. L., & Haryanto, I. (2017). *Hubungan Tingkat Pengetahuan Dan Dukungan Keluarga Terhadap Kepatuhan Diet Pasien Diabetes Mellitus Di Klinik Bhakti Husada Purwakarta*.

Inamdar, S., Kulkarni, R., Karajgi, S., Kumar, Bjm., & Inamdar Asst, S. (2013). *American Journal of Advanced Drug Delivery Medication Adherence in Diabetes Mellitus: An Overview on Pharmacist Role Address for Correspondence*.

Kementerian Kesehatan. (2018). Laporan Nasional Riset Kesehatan Dasar. In *Departemen Kesehatan R.I, Badan Penelitian Dan Pengembangan,*.

Lestari, M. A., & Amir, A. (2019). Pulmonary tuberculosis in gestational patient with diabetes mellitus in regional public hospital Dumai, Riau Province: a case report. *Jurnal Kedokteran Dan Kesehatan Indonesia*, *10*(2), 206–210. https://doi.org/10.20885/jkki.vol10.iss2.art14

Luijf, Y. M., van Bon, A. C., Hoekstra, J. B., & DeVries, J. H. (2010). Premeal Injection of Rapid-Acting Insulin Reduces Postprandial Glycemic Excursions in Type 1 Diabetes. *Diabetes Care*, *33*(10), 2152–2155. https://doi.org/10.2337/dc10-0692

PERKENI. (2015). *Pengelolaan dan pencegahan diabetes melitus tipe 2 di Indonesia 2015*.

Petersen, M. C., & Shulman, G. I. (2018). Mechanisms of Insulin Action and Insulin Resistance. *Physiological Reviews*, *98*(4), 2133–2223. https://doi.org/10.1152/physrev.00063.2017

Petrie, J. R., Guzik, T. J., & Touyz, R. M. (2018). Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. *Canadian Journal of Cardiology*, *34*(5), 575–584. https://doi.org/10.1016/j.cjca.2017.12.005

Piragine, E., Petri, D., Martelli, A., Calderone, V., & Lucenteforte, E. (2023). Adherence to Oral Antidiabetic Drugs in Patients with Type 2 Diabetes: Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*, *12*(5), 1981. https://doi.org/10.3390/jcm12051981

Priscilla, S., Malarvizhi, S., Das, A., & Natarajan, V. (2019). The level of knowledge and attitude on insulin therapy in patients with diabetes mellitus in a teaching hospital of Southern India. *Journal of Family Medicine and Primary Care*, *8*(10), 3287. https://doi.org/10.4103/jfmpc.jfmpc_622_19

Sahoo, J., Mohanty, S., Kundu, A., & Epari, V. (2022). Medication Adherence Among Patients of Type II Diabetes Mellitus and Its Associated Risk Factors: A Cross-Sectional Study in a Tertiary Care Hospital of Eastern India. *Cureus*. https://doi.org/10.7759/cureus.33074

Sartunus, R., Hasneli, Y., & Jumaini. (2015). Hubungan Pengetahuan, Persepsi dan Efektifitas Penggunaan Terapi Insulin Terhadap Kepatuhan Pasien DM Tipe II Dalam Pemberian Injeksi Insulin. *Jom*, *2*(1), 699–707.

Siti, F., & Indrawati, F. (2019). Faktor Pemanfaatan Pelayanan Kesehatan di Puskesmas. *HIGEIA JOURNAL OF PUBLIC HEALTH RESEARCH AND DEVELOPMENT*, *1*. https://doi.org/10.15294/higeia/v3i1/24747

Slattery, D., Amiel, S. A., & Choudhary, P. (2018). Optimal prandial timing of bolus insulin in diabetes management: a review. *Diabetic Medicine*, *35*(3), 306–316. https://doi.org/10.1111/dme.13525

Tan, W., Asahar, S., & Harun, N. (2015). Insulin therapy refusal among type II diabetes mellitus patients in Kubang Pasu district, Kedah, Malaysia. *Singapore Medical Journal*, *56*(04), 224–227. https://doi.org/10.11622/smedj.2014170

Marbun, V. E. (2021). Faktor-Faktor Yang Mempengaruhi Terhadap Kepatuhan Terapi Pada Penderita Diabetes Melitus Tipe 2 di Poli DM RSU Cut Meutia Kabupaten Aceh Utara Tahun 2020. *Best Journal (Biology Education, Sains and Technology)*, *4*(2), 64–70.