

The Relationship between the Duration of Type 2 Diabetes Mellitus and Diabetic Neuropathy Complications

¹Mia Anggi Anggraeni, ¹Riandi Alfin, ¹Zikran, ¹Sitti Syabariyah*

Corresponding Author: sittisyabariyah@unisa-bandung.ac.id

¹ Universitas 'Aisyiyah Bandung, Bandung, Indonesia

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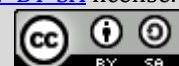
Long Suffering Time

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ABSTRACT

Diabetic neuropathy is one of the complications that often appear in patients with type 2 diabetes mellitus. This study was conducted to determine the relationship between the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy complications. This study used a quantitative research design with correlative methods and a cross-sectional approach. The sampling technique used a consecutive sampling approach within 1 month to 86 patients with type 2 diabetes mellitus at Ujungberung Indah Health Center from April to May 2023. The inclusion criteria were patients with hyperglycemia. Instruments used to measure the length of time were medical records and diabetic neuropathy screening by the Ipswich touch test. Univariate analysis used descriptive and bivariate analysis using Kendall's tau. The results showed that most patients with type 2 diabetes mellitus who suffered from diabetic neuropathy on average suffered from diabetes mellitus (DM) for more than 5 years (45.3%). Statistical analysis of Kendall's tau with $p\text{-value} = 0.000 (<0.05)$, namely there was a significant relationship between the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy. It can be concluded that there was a relationship between the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy complications.

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Introduction

Diabetes is a group of metabolic disorders characterized by high blood sugar (hyperglycemia) caused by impaired insulin secretion, insulin action, or both. Persistent hyperglycemia is associated with long-term damage or failure of organs such as the eyes, heart, kidneys, blood vessels, and nerves [1]. Type 2 diabetes mellitus is a global crisis that can threaten the health and economy of the world. Diabetes is a public health problem that is increasing worldwide, both in developed and developing countries [2].

The prevalence of diabetes mellitus is ranked in the top 10 diseases that cause death in the world. The International Diabetes Federation (IDF) estimates that in 2019 the adult-elderly age (20-79 years) there are about 463 million people in the world. The incidence rate is expected to continue to increase to 111.2 million people aged 65-79 years [3]. DM sufferers in 2030 are predicted to continue to increase to reach 578 million and as many as 700 million cases will occur in 2045 [4].

The 2017 IDF Atlas reports that Indonesia ranks sixth as the country with the highest number of people with diabetes mellitus, with approximately 10.3 million people aged 20-79 years [3]. Meanwhile, the prevalence of diabetes mellitus shows that West Java Province is ranked medium with a percentage of 1.7%. At the district/city level, the city with the most diabetes is recorded in West Java, one of which is Bandung. The incidence of diabetes has increased dramatically, the number of diabetes cases in Bandung City was 38,259 in 2022, of which 254 died from DM [5].

This high incidence of diabetes mellitus is very likely due to many things such as the absolute lack of insulin production due to autoimmune processes in type 2 diabetes mellitus the symptoms that appear are slow and progressive, so they are not detected early because the symptoms experienced by patients are often mild such as fatigue, irritability, polyuria, polydipsia, and wounds that take a long time to heal. Perkeni [6] states that the most common impact on DM patients is diabetic neuropathy, where nerve damage occurs due to weakness and damage to the capillary walls that feed the nerves. Symptoms of diabetic neuropathy vary, it may only be mild such as tingling, swelling, weakness, or severe pain, especially at night. [7].

The incidence of diabetic neuropathy in the world reaches 66% and the incidence of diabetic neuropathy in Indonesia is 58.0% [8]. Diabetic neuropathy is the most common complication, initially resulting in loss of ankle range and no vibration sensation in the lower extremities [9]. Patients with DM are sick for a long time and uncontrolled, changes in blood vessels occur. The thickening of blood vessels affects blood pressure and can slowly damage blood capillaries and nerve fibers [10].

The increasing incidence of DM can lead to several complications, including diabetic foot wounds (DFW) caused by neuropathy which, if left untreated, will lead to amputation. Foot

amputation is 10 to 30 times more common in patients with DM than in other health conditions. Therefore, it is important to screen for diabetic neuropathy before the appearance of diabetic foot ulcers as an early prevention. Early detection is important because it can prevent/stop the progression of peripheral nerve damage [11].

The duration of type 2 diabetes mellitus with high blood sugar levels affects the blood vessel walls, causing them to thicken and impacting blood pressure. This process will slowly disrupt blood capillaries & nerve fibers. The longer a person suffers from DM, the higher the risk of worsening nerve cell damage [10]. The length of time a person suffers from type 2 diabetes mellitus can cause complications of diabetic neuropathy. This is supported by the results of research [1] regarding the relationship between age, gender, and duration of diabetes with the incidence of neuropathy. Also supported by the results of research [12] regarding the length of suffering from type 2 diabetes mellitus as a risk factor for diabetic peripheral neuropathy with the results of data analysis obtained ($p\text{-value} = 0.023 < 0.05$ and $r\text{-value} = -0.438$) the majority of patients suffering from type 2 diabetes mellitus for > 5 years, this shows that there is a significant relationship between the length of suffering from type 2 DM and the risk of neuropathy.

However, in one study on physical activity with peripheral diabetic neuropathy in type 2 diabetes mellitus patients, it was found that neuropathy complaints appeared less than 1 year after being diagnosed with DM [13]. Although great progress has been made in research related to the complications of diabetic neuropathy, so far there are still cases of diabetic neuropathy, therefore this study will conduct further examinations, namely screening neuropathy using the Ipswich Touch Test (IpTT). The reason researchers use the IpTT is as the simplest method of detecting diabetic neuropathy, the latest, simple, does not have to spend money to buy tools, and the sensitivity level is good.

Nurses as health workers play a very important role in the phenomenon of diabetes mellitus. The role of nurses according to the Consortium Health Science [14] consists of the role of nursing care provider, patient advocate, educator, coordinator, collaborator, consultant, and researcher. This is in line with research that shows nurses are the professionals in an educational team in handling DM cases, namely preventive handling in the prevention of diabetic neuropathy.

Preliminary studies conducted by researchers found that the Ujungberung Indah Community Health Center in Bandung City is in the service coverage area of 1,636 people with type 2 diabetes mellitus in 2022 [5]. Researchers considered the research site based on the high distribution of patients with type 2 diabetes mellitus, besides researchers were interested in the topic of diabetic neuropathy because it was supported by preliminary study data

conducted on March 9, 2023, to 10 patients at Ujungberung Indah Health Center, 7 out of 10 patients said that they had suffered from DM for more than five years. Then, said that his feet often felt tingling, numbness, weakness, pain in the feet, and difficulty sleeping. This is interesting because there is a phenomenon related to signs and symptoms of complications from DM that may lead to diabetic neuropathy for some patients at the Puskesmas (Public Health Center).

In this study, the research question posed was What is the Relationship Between the Length of Time Suffering from Type 2 diabetes mellitus with Diabetic Neuropathy Complications at Ujungberung Indah Health Center? The purpose of this study was to determine the relationship between the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy complications at Ujungberung Indah Health Center.

Material and Methods

This research is a quantitative study using a correlative method with a cross-sectional approach. The sample size was 86 respondents. The sampling technique used consecutive sampling within 1 month (April-May 2023). Inclusion criteria in this study: clients with a history of type 2 diabetes mellitus, clients who get services at Ujungberung Indah Health Center, clients who have awareness and can communicate well, and diabetes mellitus clients who participate in Prolanis (*Program pengelolaan penyakit kronis dari BPJS Kesehatan* or specific healthcare service).

Research instruments to obtain data on the length of time patients suffer from type 2 diabetes mellitus using medical records, then to obtain neuropathy data using the IpTT, Ipswich touch test examination technique by giving a touch to the tips of the first, third, and fifth toes. Data collection starts from sampling adjusted to the inclusion criteria, writing patient data, and then screening neuropathy with the IpTT.

Validity and reliability tests were not carried out in this study because previously validity and reliability tests had been carried out in research [15] on diabetic neuropathy patients in type 2 diabetes mellitus patients with sensitivity results of 83.33% and specificity of 97.66% and said to be valid with r count 0.61 - 0.80. The instrument has been tested there is a Cronbach's Alpha coefficient of 0.819 ($p < 0.001$) from (Cronbach's Alpha > 0.060) and according to the standardized SOP [16].

Therefore, the IpTT instrument can be effectively used to evaluate sensory sensitivity in patients with diabetic neuropathy. In research for univariate analysis use descriptive analysis and for bivariate analysis, because the data is ordinal so bivariate analysis in this study will use Kendall's Tau Test. This study also has an ethical permit from the Research Ethics Committee of Universitas 'Aisyiyah Bandung with Number: 409/ KEP/01/UNISA-Bandung/V/

2023. In addition, researchers also obtained permission from relevant agencies such as the National and Political Unity and the Bandung City Health Office.

Results

The distribution of respondents according to age is dominated by the age group > 60 years with a percentage of 66.3% and the least in the age range of 30-44 years at 2.3%. The distribution of respondents according to female gender is the most, namely 56 respondents with a percentage of 65.1% and for respondents with male gender as many as 30 respondents with a percentage of 34.9%.

Data regarding the length of time suffering from type 2 diabetes mellitus was obtained through patient medical records. The distribution of respondents according to the length of time the respondents suffered from diabetes mellitus showed that most of the respondents suffered from diabetes mellitus for more than 5 years as many as 39 people (45.3%) and the fewest respondents with long-suffering from diabetes Mellitus for 1- 5 years, namely 22 people (25.6%).

Data regarding diabetic neuropathy was obtained through the Ipswich touch test examination where an examination was carried out on the foot which was examined by the researcher directly. The distribution of respondents according to the Ipswich touch test showed that 45.3% of respondents were not neuropathic and 54.7% of respondents were neuropathic.

Table 1. Characteristics of patients with type 2 diabetes mellitus in the study

Variables	f	(%)
Age		
• 30-44 years old	2	2.3
• 45-59 years old	27	31.4
• > 60 years	57	66.3
Gender		
• Male	30	34.9
• Female	56	65.1
Duration of DM		
• < 1 year	25	29.1
• 1-5 years	22	25.6
• > 5 years	39	45.3
Diabetic Neuropathy		
• Positive	47	45.3
• Negative	39	54.7

From the results of the bivariate test, it was found that the longer the time of suffering from type 2 diabetes mellitus, the higher the occurrence of diabetic neuropathy. This is shown in testing using Kendall's tau test. The results of Kendall's tau analysis with a p-value = 0.000

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which is smaller than 0.05, so H_0 is rejected, which means that there is a significant relationship (real) between the variables and H_a is accepted. Then, the correlation coefficient value of the length of suffering from type 2 diabetes mellitus with diabetic neuropathy was found to be 0.578, which means there is a strong relationship. This shows the result that there is a relationship between the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy complications at Ujungberung Indah Health Center.

Table 2. Bivariate Analysis of the Relationship Between Length of Time Suffering from Type 2 diabetes mellitus with Diabetic Neuropathy Complications

Duration of DM	Incidence of Diabetic Neuropathy				Total	<i>p-value</i>	Correlation coefficient
	Neuropathy Positive		Negative Neuropathy				
	f	%	f	%			
< 1 year	7	28.0	18	72.0	25	0.000	0.578
1-5 years	4	18.2	18	81.8	22		
> 5 years	36	92.3	3	7.7	39		
Total	47	54.7	39	45.3	86		

Discussion

Based on the results of research conducted at Ujungberung Indah Health Center by taking 86 respondents who have met the requirements as respondents, the results for the characteristics of respondents based on age grouping, most of the respondents who suffer from type 2 diabetes mellitus at Ujungberung Indah Health Center are more aged > 60 years than < 60 years. This research is in line with research conducted by La Ubo [17], who said that most respondents in the age range of diabetes mellitus sufferers 60-64 years as many as 12 people (38.7%).

Age 56-65 years is an age where there is a decrease in blood vessel flexibility which will lead to decreased vascularization of body tissues. As a person's age increases, there will be an imbalance between the production of free radicals and the free radical antidote system and body repair. Increased production of Reactive Oxygen Species (ROS) caused by hyperglycemia conditions and the process of increasing age can affect the progressivity of DM patients. In addition, there is an imbalance between the production of free radicals and the counteracting system, in the aging process there is also a decrease in the repair capacity of body cells.

Progressive exposure of ROS to cell mitochondria can induce mitochondrial dysfunction, axonal degeneration, and also neuropathy. Mitochondria play an important role in cell survival and apoptosis. ROS also reduces the production of axon neurotrophic factors (IGF1, IGF-II, NGF, and NT-3), which further impairs the ability of neurons to regenerate. In

addition, with age, mitochondrial dysfunction can occur, which will lead to decreased insulin sensitivity and pancreatic beta cell death [18].

Grouping based on gender obtained the results of respondents found at Ujungberung Indah Health Center with diabetes mellitus more women than men. This research is in line with research conducted by Simanjuntak & Simamora [12] which states that the majority of respondents with diabetes mellitus are female as many as 50 people (58.1%). This is emphasized by the results of Riskesdas in 2018 which reports that people with diabetes mellitus in Indonesia are more women than men [19].

In gender, women are more at risk of suffering from diabetic neuropathy complications because physically women have a higher chance of increasing Body Mass Index (BMI). In addition, pre-menstrual syndrome and after menopause can result in impaired body fat distribution so that it is easy to accumulate and can increase the risk of women suffering from type 2 diabetes [1]. The female hormone estrogen and estrogen receptor (ER) produced by the sex gonads have a protective role in the development of diabetes. In addition, estrogen has been shown to have pro-inflammatory and anti-inflammatory effects and ER to present to immune cells (antigen-presenting cells (APC) and T cells). These receptors have been demonstrated to modulate immune responses that may help protect organs under conditions of hyperglycemia. In older women, estrogen hormone function declines. In addition, women are usually more prone to high body mass index, menstrual cycle syndrome, and also during menopause when fat easily accumulates. These conditions prevent the transport of glucose into cells and subsequently lead to hyperglycemia.

Differences in hormone levels between women and men influence the development of neuropathic complications. High estrogen levels in women may interfere with the absorption of iodine, which plays a role in the formation of nerve myelin. High testosterone levels in men are associated with a lower risk of developing diabetes. This is due to the protective function of testosterone in the pancreas. Under glucotoxic conditions, high testosterone levels tend to decrease apoptosis in pancreatic cells. In older women, menopause can cause changes in insulin secretion, insulin sensitivity, and glucose efficiency, which can lead to further complications if glucose is out of balance. During menopause, women experience estradiol deficiency, which may result in an increased risk of diabetes [18].

Data regarding the length of time suffering from type 2 diabetes mellitus was obtained through the patient's medical record. Based on the results of the study on the length of time suffering from type 2 diabetes mellitus, it was found that more respondents at Ujungberung Indah Health Center suffered from type 2 diabetes mellitus for more than five years. This

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research is in line with research conducted by Mildawati et al. [1] that the length of time suffering from diabetes was more than 5 years for as many as 35 people (42.2%).

The longer a person has DM, the higher the risk of DM-related complications. Symptoms of diabetic neuropathy appear in 35-40% of patients with diabetes for more than 3 years and in 70% of patients with diabetes for more than 5 years. This is caused by gradual neuronal dysfunction due to prolonged hyperglycemia [20]. The occurrence of neuropathic complications is usually progressive. Prolonged high blood sugar levels lead to increased affinity for aldose reductase, which in turn leads to increased production of sorbitol. The accumulation of sorbitol increases the activity of the polyol pathway, which then causes changes in the nerve tissue, which will eventually lead to a decrease in the sensitivity of the patient's feet. Sorbitol does not pass through the cell membrane and accumulates intracellularly in the nerve tissue, leading to osmotic stress.

Osmotic stress increases intracellular fluid molarity and water flux and also causes Schwann cell damage and nerve fiber degeneration. By reducing the increase in intracellular glucose, the enzyme aldose reductase reduces the amount of glucose supply, but this can also lead to a decrease in glutathione levels, which in turn increases the production of AGEs, ultimately causing oxidative stress in neurons.

The longer a person has DM, the longer this process continues and leads to further cell damage, especially to nerves. Persistent hyperglycemia leads to non-enzymatic glycosylation reactions between proteins and reactive carbonyl and dicarbonyl compounds. The breakdown of protein glycosylation eventually results in advanced glycosylation end products (AGEs) that damage peripheral nerves and decrease neuronal vasodilation, resulting in peripheral neuropathy. The interaction of AGEs with AGE receptors can lead to inflammatory reactions and also the development of oxidative stress in various cells. The collection of AGEs reflects that elevated blood sugar levels have occurred over a long period. In the course of vascular complications in DM patients, inflammatory reactions play an important role [21].

Another study also said that most patients who experienced diabetic neuropathy had suffered from type 2 diabetes mellitus for more than 5 years (92.3%). This study is in line with research by Amelia et al. [22], Abdissa et al. [23] and Sendi et al. [24]. In addition, diabetic neuropathy complications are more common in people who have suffered from DM for more than five years. Patients with DM that lasts more than 5 years increase the risk of diabetic neuropathy four to five times compared to DM that lasts less than five years. The duration of DM disease is directly proportional to the risk of complications, i.e. the longer a person has diabetes mellitus, the higher the risk of complications.

The duration of type 2 diabetes mellitus and high blood sugar affect the blood vessel wall, causing the blood vessel wall to thicken and affect blood pressure. The process can damage blood capillaries and nerve fibers. The longer a person has DM, the greater the risk of worsening nerve damage. Chronic hyperglycemia in the early stages of type 2 diabetes can trigger changes in cell biochemical homeostasis affecting small nerve fibers, and as the disease progresses, large nerve fibers can result in a decrease in nerve conduction velocity.

Prolonged elevation of blood sugar levels can also result in the activity of the polyol pathway that can reduce myoinositol levels and increase the accumulation of sorbitol in nerve cells. This condition will interfere with signal transduction in the nerves. Another factor is that prolonged hyperglycemia will trigger the formation of AGEs. This process causes damage to body proteins, including nerve cells. AGEs and sorbitol formed will reduce nitric oxide function, reduce vasodilation, reduce blood flow to the nerves, and reduce myoinositol levels in nerve cells which contribute to neuropathy [10].

Based on the results of the examination carried out using the Ipswich touch test, the results of respondents with poor sensitivity were obtained. It can be concluded that someone who experiences neuropathy is more. This research is in line with research conducted by Rahmi et al. [10] on someone who experienced more neuropathy was 33 people.

DM is a cause of neuropathy through increased oxidative stress leading to increased AGEs, polyol accumulation, decreased nitric oxide, impaired endothelial function, impaired Na/K-ATPase activity, and homocysteinemia. In hyperglycemia, glucose combines with proteins to form glycosylated proteins, which can be damaged by free radicals and fats, forming AGEs that then damage sensitive nerve tissues. Diabetic peripheral neuropathy is nerve damage caused by diabetes. Over time, high blood sugar damages the nerves. Nerve damage is most common in diabetics who have had diabetes for many years. Controlling sugar levels is one way to prevent nerve damage [13].

Hypothesis testing in this study regarding the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy complications at Ujungberung Indah Health Center. So it can be concluded that there is a relationship between the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy complications at the Ujungberung Indah Health Center. The results of this study are by the theory that says that long-suffering from diabetes is one of the factors for neuropathy complications. The onset of diabetes mellitus will affect small nerve fibers which then with the duration or length of suffering will be followed by large nerve fibers and then associated with reduced nerve conductivity [11].

Of the 86 research respondents, 39 people experienced neuropathy complications with a duration of more than 5 years. This is in line with the theory [25] that the length of time diagnosed with DM is related to a decrease in pancreatic beta cell function so that it will cause complications which generally occur in patients with a length of illness of 5-10 years. So it can be concluded here that the longer a person has type 2 diabetes mellitus, the greater the risk of diabetic neuropathy complications that occur. The results of this study are in line with research conducted by La Ubo [17]. The results of the study showed that there was a long relationship between type 2 diabetes mellitus and the incidence of diabetic polyneuropathy complications. The difference between this study and the study is in sampling techniques, number of samples, time and place, and data analysis techniques.

However, it is not in line with research conducted by Selano [26] showing that there was no relationship between the duration of suffering and the incidence of diabetic neuropathy. This is because the factors that affect the severity of peripheral neuropathy in DM patients are not only the length of suffering but also the age, duration of DM, HbA1C, lipid levels, and so on.

The long duration of type 2 diabetes mellitus less than 5 years but already experiencing diabetic neuropathy is influenced by several mechanisms that contribute to the development of nerve damage, one of which is the blood glucose control of DM patients. The worse the glucose control, the greater the risk of developing severe neuropathy. The patient's blood glucose control is described by HbA1C levels. HbA1C levels can provide an overview of the blood sugar control of patients with DM in 1 -3 months. Poor blood sugar control can lead to chronic hyperglycemia conditions. Chronic hyperglycemia contributes significantly to axon damage which is the basis for the development of peripheral neuropathy in DM patients [26].

The degenerative aging process affects the general changes and diseases accompanying the aging process. People with diabetes should pay more attention to their health to prevent complications. Duration of diabetes mellitus of more than 5 years, the presence of foot deformities, and visual impairment due to uncontrolled blood sugar and visual impairment can affect the management of ulcer prevention such as difficulty in foot care. People with DM who have had ulcers in the past are at risk of developing ulcers again. This may be because many people with diabetes do not understand how to prevent recurrent ulcers, which are associated with an unhealthy lifestyle that can worsen their health [28].

The process of DM development in neuropathy is usually progressive. Long-term high blood sugar leads to the accumulation of sorbitol, which can increase the activity of the polyol pathway and cause changes in nerve tissue. These changes contribute to impaired nerve signaling that leads to decreased sensitivity in the feet in patients with type 2 DM. This results

in a lack of pain sensitivity, heat, and mechanical injury, and diabetics do not realize that they have sustained some foot injuries that can result in foot ulcers [12].

The results showed that the highest age was more than 60 years of diabetes mellitus patients at Ujungberung Indah Health Center. Elderly people who are healthy, productive, and independent have a positive impact. Conversely, if the increase in the number of elderly people is not in good health, it will increase the burden on the productive age population. The problem most often faced by the elderly is health problems, one of which is diabetes mellitus. The elderly with DM for a long time generally have a poor quality of life because it has a negative influence on the physical and psychological of the sufferers. DM sufferers are usually unable to carry out daily activities and cannot carry out social activities [28].

Older people with DM who are cared for by their family during their illness do better than those who are cared for by others. People who are in a supportive environment do much better. Support from family provides practical help to those suffering from the disease and helps reduce the burden of living with the disease. Family members play an important role in the progress of the patient's spirit, showing affection and relieving pressure [29].

Conclusion

After the research was conducted, it was found that the length of time suffering from DM was mostly more than 5 years, and in the examination results many respondents with positive results of diabetic neuropathy at Ujungberung Indah Health Center. So, there is a relationship between the length of time suffering from type 2 diabetes mellitus with diabetic neuropathy complications. Thus, this study can be useful as an effort to prevent diabetic neuropathy by conducting initial screening using the Ipswich touch test and can be used as a benchmark for improving further research that is still related to diabetes mellitus.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Authors



Mia Anggi Anggraeni is an emerging researcher with a strong academic background in health sciences. She earned her bachelor's degree from Universitas Aisyiyah Bandung, where she developed foundational knowledge and skills in healthcare and research. As a research member in this study, Mia contributed her expertise and dedication to advancing the understanding of critical health topics. Her passion for healthcare research reflects her commitment to improving community health outcomes. She remains actively engaged in collaborative projects that aim to make a meaningful impact in the field of health sciences. (mail: miiaanggi26@gmail.com).



Riandi Alfin is a dedicated junior lecturer at the Faculty of Health Sciences at Universitas Aisyiyah Bandung and also serves as a visiting lecturer at Universiti Teknologi Mara (UiTM) in Malaysia. With a strong focus on nursing education, her primary research interests lie in medical-surgical nursing, where he explores innovative approaches to enhance patient care and nursing practices. Through his academic roles in Indonesia and Malaysia, Raindi has fostered cross-border collaborations, contributing to the enrichment of nursing education and research in both countries. His work emphasizes the importance of evidence-based practices in nursing, and he is committed to mentoring students and fellow researchers to advance the field. (mail: riandi.alvin@unisa-bandung.ac.id).



Zikran is a junior lecturer at the Faculty of Health Sciences, Universitas Aisyiyah Bandung, where he is actively involved in teaching and research in nursing. His academic work focuses on improving nursing practices and fostering a deeper understanding of the challenges and opportunities within healthcare delivery. Zikran is passionate about advancing the nursing profession by participating in research initiatives that explore innovative solutions for patient care and healthcare education. He values collaboration and aims to contribute meaningfully to the academic and professional nursing community. (mail: zikran.m@gmail.com).



Dr. Sitty Syabariyah, S.Kp., MS. Biomed is a senior lecturer at the Faculty of Health Sciences of Aisyiyah University of Bandung. Doctoral degree obtained from the University of Indonesia. Her expertise is in nursing, health, hospital, and risk management. She has published many articles in international journals. She also works as a visiting senior lecturer at the Universiti Teknologi Mara (UiTM) Malaysia. She is the Reviewer of the Journal of Health Sciences and Medical Development. (email: sittisyabariyah@unisabandung.ac.id).