



Risk Factors of Patients with Gangrene Pedis with Type 2 Diabetes Mellitus Followed by Anti-Diabetic and Insulin Drug Therapy

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ABSTRACT

Introduction: Gas gangrene is an extremely lethal infection in the inner soft fingers, commonly caused by gram-positive bacteria such as *Staphylococcus aureus* or *Clostridium perfringens*, and has symptoms similar to those of type 2 diabetes mellitus, including muscle necrosis and myonecrosis. Hyperglycemia and glucosuria are two symptoms of diabetes mellitus, which is a group of symptoms induced by an imbalance between carbs, lipids, and proteins due to absolute and relative insulin insufficiency.

Purpose: secondary data analysis at Bhayangkara Kediri Hospital during the period of January 2021 - March 2022 to characterize the type II diabetic patients who suffered from gas gangrene of the feet.

Method: This investigation is a cohort retrospective design observational study (Non-Experimental Design). Type II Diabetic Mellitus patients treated at Bhayangkara Kediri Hospital between January 2021 and March 2022 made up the study's sample.

Results: The p value for Gas Treatment in cases of Wagner Grade 2 or 3 Gas Gangrene of the Feet is 0.2199. Wagner Grade and Gas Treatment for Gas Gangrene of the Feet are not significantly related to debridement action (n = 8) or the most common bacteria (*Pseudomonas aeruginosa*; n = 4).

Conclusion: If a patient with pedis gas gangrene has a history of not consistently regulating their disease because of the effects of diabetes mellitus medication, they are more likely to experience progressive worsening of their condition as a result of metabolic neuropathy. The results of treatment vary from patient to patient.

Keywords: Gas gangrene, Diabetes Mellitus Type II, Debridement, *Pseudomonas aeruginosa*.

INTRODUCTION

An extremely lethal infection in the interior soft tissues of the fingers, gangrene gas is typically caused by gram-positive bacteria like *Staphylococcus aureus* or *Clostridium perfringens*. This condition has been linked to the rising prevalence of type 2 diabetes mellitus [1]. (Hyperglycemia and glucosuria are two symptoms of diabetes mellitus, which is a group of symptoms induced by an imbalance between carbs, lipids, and proteins due to absolute and relative insulin insufficiency [2]. Insulin resistance causes type II diabetes mellitus by preventing glucose from being absorbed by the body and leading to a shortage of beta pancreatic cells, which in turn reduces insulin release and activity. Patients with Type II DM are at increased risk for developing long-term consequences such cardiovascular disease and stroke, kidney failure, blindness, and diabetic gangrene [3]. In the degenerative bone disorder known as avascular necrosis/osteonecrosis, cellular components of bone die because of inadequate blood flow to the subchondral sulcus. Epiphyseal fractures of long bones are common in overloaded joints or in areas where *Staphylococcus aureus* germs have invaded the surrounding tissue [4]. The osteonecrosis known as Multiple Avascular Necrosis (MAVN) is a complication of vascular problems of the bones that leads to the death of spinal cord cells, osteocytes, and snake trabek cells to the point where the necrotic segments of bone collapse [5]. The December 2021 statistics show that only about 1000 cases of Gangrene pedis occur annually in the United States. However, in less developed countries like India, where access to health care and antibiotics is limited, the disease is more common and has a mortality rate of over 67% among the 8,000 population in India and Vietnam in 2019. [6]. In 2012, diabetes mellitus was listed as one of the ten most prevalent noncommunicable diseases by the Ministry of Health of the Republic of Indonesia. With 21,159 new cases in 2017, diabetes mellitus rose to the top spot as the leading NCD in Semarang City in 2017. [7]. According to epidemiological studies [8], diabetic gangrene causes over a million amputations annually in Indonesia. In Indonesia, 15% of the population has diabetic gangrene, and

30% of those people will need an amputation [9]. Another study found that patients with a history of type II diabetes mellitus for longer than five years had a risk level two times greater for developing peripheral neuropathy due to multiple osteonecrosis in patients with gangrene pedis acquired diabetic ulcer [10]. Ten percent of those diagnosed with multiple osteonecrosis in the United States are between the ages of 30 and 65, and males are more likely to be affected than females. Among the 3,125 people living in the United States, 90% are women and the average patient age is 65. [11]. Type II diabetes mellitus, also known as gangrene pedis, continues to be a serious health issue in Indonesia, a developing country, due to the high prevalence of both diabetes and poverty [12]. Microorganisms that are facultative anaerobic bacteria, specifically *Staphylococcus aureus*, where bacteria enter through soft tissue that occurs in the need for diabetic gangrene [13], to cause peripheral neuropathy due to damage from the blood supply to bone cells that produce death from many cells bone in some parts or compartments and is one of the potential causes of Multiple Avascular Necrosis in Gangrene Pedis patients [14].

Important and prompt treatment for gangrene pedis includes antibiotics, wound debridement with the help of a surgeon, intravenous fluid resuscitation, intensive care unit monitoring, and hyperbaric oxygen as an adjunctive therapy [15]. In addition to the aforementioned irritant drugs, such as iodine tincture and mercury bin-iodide, local astringent administration, such as boric acid and tannic acid, and antibacterial agents like neobakrin ointment, can be given as a treatment for gangrene pedis, though their use should be restricted and supervised by a surgeon [16]. Antibiotics can kill the germs that cause gangrene in the feet. In the context of microorganisms like bacteria and fungi, antibiotics are substances that have been produced to inhibit their growth. Prophylactic therapy for multiple osteonecrosis, also known as endoprosthetic replacement on afflicted bones and soft tissue, can be performed as either preventative medicine or reconstructive surgery. Decompression of the nucleus of the femoral head is the most commonly performed prophylactic operation, with the dual goals of

relieving venous congestion and promoting healing. Joint arthroscopy revealing varying degrees of condral folds and a picture of joint degeneration with joint collapse due to pedis gangrene can confirm the need for decompression in the malleoli pedis to improve mechanical support and promote the healing of avascular necrosis caused by Staphylococcus aureus bacteria in gangrene pedis [17]. Prophylactic therapy with pencillin and clindamycin, which has a broad spectrum against germs in the Streptococcal group [18], is recommended for patients with avascular necrosis leading to gangrene of the feet [19].

Leg ischemia occurs when blood flow is impaired. Patients with gangrene pedis may encounter similar signs and symptoms. Leg pain is a common complaint among patients, especially when they have to spend extended periods of time standing, walking, or performing other types of physical activity. The arcus pedis is prone to nighttime and resting pain [20]. The skin takes on a pucar, thin, glossy, or bluish hue upon close inspection. Ulcers that are difficult to cure and eventually become gangrene are detected, and it is difficult to feel a pulse in the poplitea or posterior tibialis [21]. Patients with gangrene and peripheral neuropathy from avascular necrosis typically have abnormalities and sclerotic alterations in the pedis, most noticeably in the region of the malleolus bone [22]. The nectrotic process in the bone in the

femur on the side who gets pedis gangrene, commonly called arthritic pain, is the likely cause of the pain felt by patients, particularly when they are preparing to walk [23].

METHODS

This study employs a cohort retrospective design, making it an observational study (Non-Experimental Design). The study took place at Bhayangkara Kediri Hospital's Laboratory and Medical Record Admission Center. Research began in June of 2022 and continued until the fall of that year. The patients with Gangrene Pedis Gas who were treated at Bhayangkara Kediri Hospital between January 2021 and March 2022 were used as the study population. Patients diagnosed with Type II diabetes and treated at Bhayangkara Kediri Hospital between January 2021 and March 2022 comprised the study's sample.

Data gathered descriptively were analyzed using the Pearson Chi-square correlation test on a qualitative categorical data scale in SPSS. The significance level of the test was set at 5%, or = 0.05, to ensure that the results were reliable.

RESULTS

Research Result Descriptive Statistics

TABLE 1: Descriptive Statistics

		n	%	Mean	Stdev
Wagner Grade	Grade I	1	8.33		
	Grade II	4	33.33		
	Grade III	1	8.33		
	Grade IV	3	25.00		
	Grade V	3	25.00		
Gender	Man	7	58.33		
	Woman	5	41.67		
Bacterial Culkur	Pseudomonas aeruginosa	8	66.67		
	Staphylococcus aureus	3	25.00		
	Streptococcus pyogenes	1	8.33		
old DM II	Less than 1 Year	7	58.33		
	1 year and above	5	41.67		

Osteomyelitis	Negative	8	66.67		
	Positive	4	33.33		
Avascular necrosis	Negative	7	58.33		
	Positive	5	41.67		
Charcote	Negative	9	75.00		
	Positive	3	25.00		
DM therapy	Glibenclamide	1	8.33		
	Glimepiride	1	8.33		
	Long & Rapid Acting	1	8.33		
	Metformin	4	33.33		
	Rapid Acting Insulin	5	41.67		
Diabetic Foot Therapy	Amputation	4	33.33		
	Debridement	8	66.67		
Age		12		42.08	17.79
Hb		12		10.50	1.93
Leukocyte		12		204916.67	86379.14
Neutrophils		5		10300.00	1717.56
LED		5		21.40	1.67
GDA		12		295.42	42.61
HbA1c		12		8.33	0.49

Wagner Grade Comparison

The following table displays descriptive data from a comparison of Wagner Grades..

TABLE 2: Wagner Grade Comparison Test Results

		N	Mean	Std. Deviation
Hb	Grade I	1	10.00	.
	Grade II	4	10.50	1.29
	Grade III	1	10.00	.
	Grade IV	3	11.67	2.08
	Grade V	3	9.67	3.21
Leukocyte	Grade I	1	288000.00	.
	Grade II	4	176250.00	88635.49
	Grade III	1	110000.00	.
	Grade IV	3	256666.67	50083.26
	Grade V	3	195333.33	113975.14
Neutrophils	Grade I	0	.	.
	Grade II	2	11000.00	1414.21
	Grade III	1	9500.00	.
	Grade IV	1	12000.00	.
	Grade V	1	8000.00	.
LED	Grade I	0	.	.
	Grade II	2	20.50	0.71

	Grade III	1	20.00	.
	Grade IV	1	24.00	.
	Grade V	1	22.00	.
GDA	Grade I	1	295.00	.
	Grade II	4	270.00	44.16
	Grade III	1	280.00	.
	Grade IV	3	343.33	32.15
	Grade V	3	286.67	32.53
HbA1c	Grade I	1	8.00	.
	Grade II	4	8.25	0.50
	Grade III	1	8.00	.
	Grade IV	3	8.33	0.58
	Grade V	3	8.67	0.58

Data source: Appendix 3

Wagner Grade Cross Tabulation

The results of Wagner grade Cross abulation can be seen in Table 5.3

TABLE 3: Cross-Tabulation Results between Wagner Grade and Gender

Wagner Grade	Gender		Total	p
	Man	Woman		
Grade I	0	1	1	0.489
Grade II	3	1	4	
Grade III	0	1	1	
Grade IV	2	1	3	
Grade V	2	1	3	
	7	5	12	

Wagner Grade is associated with gender with a p value of 0.489, according to the results of the Association Test. As $p > 5\%$, we can conclude

that H_0 is correct. This indicates that a weak association between gender and the Wagner Grade variable.

TABLE 4: Cross-Tabulation Results between Wagner Grade and Bacterial Culture

Wagner Grade	Bacterial Cukltur			Total	p
	Pseudomonas aeruginosa	Staphylococcus aureus	Streptococcus pyogenes		
Grade I	1	0	0	1	0.805
Grade II	3	1	0	4	
Grade III	1	0	0	1	
Grade IV	1	1	1	3	
Grade V	2	1	0	3	
	8	3	1	12	

The H_0 hypothesis is supported since the p value of the Association Test between Wagner Grade and Bacterial Culture is greater than $=5\%$. Thus,

the correlation between Wagner Grade and the bacterial-culture-induced variable is quite small.

TABLE 5: Cross-Tabulation Results between Wagner Grade and Long DM

Wagner Grade	old DM II		Total	P
	Less than 1 Year	1 year and above		
Grade I	1	0	1	0.187
Grade II	3	1	4	
Grade III	1	0	1	
Grade IV	2	1	3	
Grade V	0	3	3	
	7	5	12	

The significance level (p) of the correlation between Wagner Grade and Long DM is 0.187, which means that the H0 hypothesis is supported. This suggests that the old DM's weak correlation accounts for the Wagner Grade fluctuation.

TABLE 6: Results of Cross-Tabulation between Wagner Grade and Complications of Osteomyelitis

Wagner Grade	Osteomyelitis		Total	P
	Negative	Positive		
Grade I	1	0	1	0.622
Grade II	3	1	4	
Grade III	1	0	1	
Grade IV	2	1	3	
Grade V	1	2	3	
	8	4	12	

The significance level (p) of the association between Wagner Grade and osteomyelitis complications is 0.622, which is above the critical value of =5% and so supports the acceptance of the null hypothesis (H0). Hence, the Wagner Grade variable is unrelated to Osteomyelitis Complications.

TABLE 7: Results of Cross-Tabulation between Wagner Grade and Complications of Avascular necrosis

Wagner Grade	Avascular necrosis		Total	P
	Negative	Positive		
Grade I	1	0	1	0,055
Grade II	4	0	4	
Grade III	1	0	1	
Grade IV	1	2	3	
Grade V	0	3	3	
	7	5	12	

The significance level (p) for the association between Wagner Grade and Avascular Necrosis Complications is $\geq 5\%$, hence the null hypothesis (H0) is rejected. What this suggests is that the Wagner Grade variable is unrelated to Avascular Necrosis Complications.

TABLE 8: Cross-Tabulation Results between Wagner Grade and Charcott

Wagner Grade	Charcott		Total	P
	Negative	Positive		
Grade I	1	0	1	0.299
Grade II	4	0	4	
Grade III	0	1	1	
Grade IV	2	1	3	
Grade V	2	1	3	
	9	3	12	

The wagner Grade–Charcott Association Test yielded a p value of 0.299, which is statistically significant ($p > 5\%$) and so supports the null hypothesis (H_0). This suggests that the connection between Charcott's Wagner Grade variable and anything else is quite weak.

TABLE 9: Cross-Tabulation Results between Wagner Grade and DM therapy

Wagner Grade	DM therapy					Total	p
	Glibenclamide	Glimepiride	Long & Rapid Acting	Metformin	Rapid Acting Insulin		
Grade I	0	0	0	1	0	1	0,525
Grade II	0	0	0	2	2	4	
Grade III	0	0	0	0	1	1	
Grade IV	0	0	0	1	2	3	
Grade V	1	1	1	0	0	3	
	1	1	1	4	5	12	

Based on the results of the Association Test between wagner Grade and DM therapy has a p value of 0.525, Since the significance value (p) is greater than $\alpha = 5\%$ then the H_0 hypothesis is accepted. This means that the Wagner Grade variable with DM Therapy has an insignificant association.

TABLE 10: Results of Cross-Tabulation between Wagner Grade and Gangrene Pedis Therapy

Wagner Grade	Diabetic Foot Therapy		Total	P
	Amputation	Debridement		
Grade I	0	1	1	0,199
Grade II	0	4	4	
Grade III	0	1	1	
Grade IV	2	1	3	
Grade V	2	1	3	
	4	8	12	

Wagner Grade and diabetic foot therapy are associated with a p value of 0.2199, according to an association test. As $p > 5\%$, we can conclude that H_0 is correct. This indicates that the Wagner Grade variable is not significantly linked to diabetic foot therapy.

DISCUSSION

Definition and Characteristics of the Gas That Causes Gangrene in the Feet Cohort retrospective design (Non Experimental Design) method was used to analyze patients with type II diabetes mellitus at Bhayangkara Kediri Hospital from January 2021 to March 2022; this involved correlating the number of patients suffering from gangrene pedis gas at Bhayangkara Kediri Hospital with several predetermined variables. The study's authors concluded that the H0 results were "acceptable / no results," indicating that the therapeutic targets and efficacy of the treatment were on target. Univariate analysis showed that the average number of patients with prolonged diabetes > 2 years was 52.3% and dominated by mostly male sex 50.6% with p 0.05 or H1 is acceptable; however, not all of the listed variables were consistent with the research conducted by Henry Setiawan using the secondary data observation method. According to the study's findings, gangrene pedis gas is caused by neuropathy and vascular diseases and manifests itself as an infection, ulceration, or deep digestion of connective tissue. There is a high probability of worsening progressiveness in patients with a history of not routinely controlling due to DM treatment suffered gangrene pedis gas condition, one of which is causing metabolic neuropathy with varying therapeutic outcomes of each patient due to the varying degrees of tissue damage each patient experiences from pedis gangrene gas. Wounds heal more quickly in women (20-40%) compared to men (5%). [24].

Hasneli (2017) studied the detection and evaluation of blood sugar levels in diabetic patients, and found that the median value for blood sugar in a randomly selected sample of 34 DM patients was 311.5 mg/dL, with minimum and maximum values of 195 mg/d: and 500 mg/dL, respectively; normal values of fasting blood sugar levels are 100 mg/dL. Patients with pedis gangrene gas were obtained with median myomic values of 3 and a maximum of 9 in the left leg, 4 and 9 in the right leg; this suggests that high blood sugar levels in diabetic patients may contribute to the sensitivity of the feet in people with type II diabetes mellitus; however, the fact that these values vary from patient to patient

indicates that the symptoms are not clinically significant or H0 is acceptable [25].

There are three types of neuropathy that can affect people with diabetes: sensory, motor, and autonomic. Atrophic, cold, and swollen nails describe the gangrene pedis that occurs in patients with type II diabetes mellitus due to vascular irregularities in the form of ischemics caused by the process of macroangiopathy and diminished tissue circulation. Patients' toes and legs become infected, and later on they develop Avascular Necrosis, Charcot disease, or osteomyelitis as a result [26]. The Wagner-Meggitt classification, developed in the 1970s, was used to classify individuals suffering from pedis gangrene. Degrees 4 and 5 respectively represent pedis gangrene affecting the soles and the entirety of the foot [27]. Complications and clinical signs of pedis gangrene vary from patient to patient, depending on the underlying cause of the illness. Anaerobic bacteria, most commonly *Clostridium difficile* and *Pseudomonas aeruginosa*, cause gangrene in persons with type II diabetes mellitus by producing gas and triggering the development of angiopathy [28]. Wagner-Meggitt grade of diabetic foot/gangrene pedis, bacterial culture, and consequences of diseases are theoretically associated; nevertheless, the incidence of each patient is variable in outcome, causing H0 to be acceptable or inconsequential.

Ischemia occurs when blood flow is impaired to the legs. Neuropadi anomalies occur at multiple phases in this case. Patients frequently report leg pain when they are upright, whether they are walking or standing. The feet are obviously cold, and it's tough to feel a pulse in the popliteal or posterior tibial arteries. The patient's legs had developed ulcers from the constant, localized pressure. Since the ulcer is so stubborn, gangrene will develop if left untreated. Bed rest, blood sugar regulation via diet, insulin, or oral antidiabetic drugs, and debridement of the leg wounds are all potential treatments for gangrene gas. Application of either culture-specific or broad-spectrum antibiotic creams or ointments. Dipyridamol, a kind of aspirin, can be used to reduce the risk of angiopathy. According to the current grade or medical indications, patients

with gangrene pedis may undergo surgical techniques including prompt amputation, debridement, and drainage [29]. According to the findings of the existing studies, there are indications, varied outcomes, and the same goal when it comes to the action or therapy given to patients with gangrene pedis.

The results of this study provide an overview of the profile of patients with gangrene pedis and type II diabetes mellitus in the secondary data at the hospital Bhayangkara Kediri during the specified period and allow one to see the number of patients who have been entered according to the specified variable criteria, so it can be classified as a descriptive study.

The small number of patients who existed and had pus cultures performed meant that the required sample size (n) for retrospective analytical investigations was not satisfied, hence the study's results can only be summarized descriptively statistically.

Further research is needed to analyze the effect of pedis gangrene therapy with type II diabetes mellitus to determine which therapy is most effective or influential on the patient according to their grading

CONCLUSION

Based on the results of the research and discussion in this study, the following conclusions can be drawn:

- Patients with type II diabetes mellitus who have blood sugar levels that are too high may experience diminished foot sensitivity..
- Patients with a history of not routinely controlling DM treatment are more likely to experience a progressive worsening of their pedis gangrene gas condition. This is because the neuropathy metabolic that results from the tissue damage experienced by each patient of pedis gangrene gas results in varying therapeutic outcomes.
- According to the study's findings, *Pseudomonas aeruginosa* is the most harmful bacteria, with n = 4 cases. In addition to debridement, the most common treatment for patients with gangrene pedis gas. Some

patients with a high grading decide against amputation and opt instead for debridement.

- Ischemic vascular illnesses such as Avascular Necrosis, Charcot disease, and/or Osteomyelitis manifest in patients with type II diabetes mellitus who develop gangrene pedis. Based on the data collected, avascular necrosis was shown to be the most common complication with a total of n = 5.
- The results of this study fit the definition of a descriptive study because they provide a snapshot of the demographics and clinical characteristics of patients with gangrene pedis and type II diabetes mellitus in the secondary data from the hospital Bhayangkara Kediri over the specified time frame and according to the variable criteria that were specified.

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