Exploring the Impact of Diabetes on Feet: Analysis of Foot Ulcers with a Focus on Eczema-Related Considerations

Namlhun Jachung

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Exploring the Impact of Diabetes on Feet:
Analysis of Foot Ulcers with a Focus on Eczema-Related Considerations

A Thesis Presented

by

Namihun Jachung

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Abstract

Diabetes mellitus, a chronic metabolic disorder, has far-reaching consequences on various organ systems, with the lower extremities being particularly susceptible to complications. This study delves into the profound effects of diabetes on the feet, specifically examining the interplay between diabetes-induced foot ulcers, and potential complications arising from coexisting eczema. Two distinct experiments were designed to investigate critical aspects of this complex relationship.

The first experiment aims to compare Transepidermal Water Loss (TEWL) levels among diabetic patients with and without eczema. The study involves a cohort of diabetic patients, stratified based on the presence or absence of eczema, and measured TEWL levels. Preliminary findings suggest an increase in TEWL is a characteristic of eczema; however, it is currently unknown whether TEWL can be used as a biomarker in regards to DFU healing.

The second experiment focused on the microbial landscape of foot ulcers in diabetic patients, exploring the prevalence of bacterial infections and assessing sensitivity to antibiotic resistance, particularly in the context of coexisting eczema. A cohort of diabetic patients with foot ulcers will be subdivided based on the presence or absence of eczema, and microbiological samples will be collected from the ulcer sites. Bacterial isolates were then subjected to antibiotic susceptibility testing to delineate the resistance profiles. The results revealed distinctive microbial antibiotic resistance in ulcers with eczema, indicating a potential link between diabetic foot ulcers and microbial colonization. This project underscores the importance of tailored testing and treatment strategies for diabetic foot ulcers based on concurrent dermatological conditions.
Background

The prevalence of diabetes in the US is overwhelming in the 21st century. Diabetes is a chronic metabolic disorder characterized by elevated blood sugar levels. Between 2001 and 2020, 11.3% of the US population had this disease, both diagnosed and undiagnosed. The majority of this development can be attributed to an increase in Type 2 diabetes associated with obesity. Examining the historical context of diabetes allows us to appreciate the progress made in our understanding and management of this disease, as well as notice what information we could further gather to make developments.

Diabetes mellitus (DM) dates back to ancient Egypt, India, and China, as well as evident in literature from ancient Greek and Arab physicians. Many discoveries have been made that extend our understanding of causes and effective treatments. Mellitus was added during the 17th century to describe the extremely sweet taste of the urine. In 1923 Frederick Banting and John MacLeod were able to discover the function of a hormone secreted by the pancreas which allows cells to utilize sugar and lower blood sugar levels. Himsworth in 1936 defined 2 different types of Diabetes as “insulin-sensitive” and “insulin-insensitive”, which are now known as Type 1 and Type 2. Type 1 Diabetes (T1DM) is an autoimmune disease in which T-cells attack pancreatic Beta cells that produce insulin. Type 2 Diabetes (T2DM) is due to a reduction in insulin production and a gained resistance to insulin. Throughout the 20th century, important progress has been made regarding the availability and administration of insulin devices.

There are numerous risk factors for Diabetes, such as genetics, race, age, weight, physical activity, blood pressure, cholesterol, and diet. People can inherit a predisposition to the disease, however there also has to be an environmental trigger. With T1DM most people inherit risk
factors from both parents; genetically the susceptibility locus to the HLA class II genes at chromosome 6p21 compensates for 30-50% of T1DM risk. There is still much to ascertain about genetic risk for Diabetes; however, a substantial amount of research indicates that, at least in terms of shared variants, the structure of genes causing an elevated risk of type 2 diabetes is similar among ethnic and racial populations.

Diabetes does not affect all racial and ethnic groups equally. Studies consistently show variations in the prevalence of diabetes among different populations. In the United States, for example, African Americans, Hispanics, Native Americans, and certain Asian-American subgroups have higher rates of diabetes compared to non-Hispanic whites. When discussing race as a factor for diabetes it is important to keep in mind healthcare disparities and socio-economic factors as this is a multifaceted issue. Racial and ethnic minorities often face socio-economic limitations, including lower income levels, limited educational opportunities, and reduced access to healthcare. These factors can contribute to a higher risk of developing diabetes and experiencing complications due to barriers to accessing preventive care and effective management. Limited access to healthcare services, cultural barriers, and implicit biases within the healthcare system can affect the diagnosis, treatment, and management of diabetes. Minority populations may face challenges in receiving timely and appropriate care, leading to uncontrolled diabetes and increased complications.

The relationship between age and diabetes is also a critical aspect of understanding the epidemiology, risk factors, and management of this prevalent metabolic disorder. Diabetes can affect individuals across the lifespan, but age is a significant factor that influences both the likelihood of developing diabetes and the management strategies employed. Diabetes prevalence

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6 Genetics of type 1 diabetes (2012)
7 Race/ethnic difference in diabetes and diabetic complications (2013)
8 Associations of age at diagnosis and duration of diabetes with morbidity and mortality (2022)
tends to increase with age. According to global and national health statistics, the risk of developing diabetes rises progressively as individuals move into older age groups. While Type 1 diabetes can occur at any age, Type 2 diabetes is more commonly diagnosed in middle-aged and older individuals. The prevalence of diabetes is notably higher in adults aged 65 and older.\(^9\) Gestational diabetes, a form of diabetes that occurs during pregnancy, is influenced by maternal age. Advanced maternal age is associated with an increased risk of gestational diabetes.\(^10\) This condition not only affects the health of the mother during pregnancy but also poses risks for the development of Type 2 diabetes later in life. Diabetes can lead to various complications that may be exacerbated by aging. Cardiovascular disease, neuropathy, retinopathy, and kidney disease are examples of complications that may have a more significant impact on older individuals.\(^11\) Managing these complications in the context of age-related health concerns poses unique challenges for healthcare providers.

The relationship between weight and diabetes has been well explored. Weight, particularly excess body weight and obesity is a significant contributor to the onset and progression of Type 2 diabetes, while it also plays a role in the management of Type 1. Excess body weight, especially in the form of visceral fat, contributes to insulin resistance, a condition where the body's cells do not respond effectively to insulin. Insulin resistance is a key factor in the development of Type 2 diabetes, as it leads to elevated blood sugar levels.\(^12\) Central obesity, characterized by excess fat around the abdominal area is particularly associated with insulin resistance, as fat cells contribute to inflammatory cytokine production that can disrupt insulin action.\(^13\) Physical activity is another risk factor for Diabetes, which relates to weight. Physical

\(^9\) Type 2 diabetes (2023)
\(^10\) Gestational diabetes mellitus (2019)
\(^11\) Associations of age at diagnosis and duration of diabetes with morbidity and mortality among older adults (2022)
\(^12\) Obesity and diabetes-not only a simple link between two epidemics (2018)
\(^13\) What causes the insulin resistance underlying obesity? (2012)
activity contributes to better metabolic health and maintains a healthy weight. One of the key physiological responses to regular exercise is the modulation of insulin sensitivity, a critical factor in glucose homeostasis. Physical activity stimulates muscle glucose uptake, which is mediated by insulin-independent mechanisms. The contraction of muscles enhances glucose transport and facilitates an increased insulin sensitivity over time. Changes in adipose tissue also promote the release of adipokines and reduce circulating free fatty acids which are a known factor in insulin resistance. Additionally, recent studies appear to support the benefits of both resistance training and aerobic exercise for the prevention and treatment of health issues. However, there is still much to learn about the relationships between exercise and diabetes, and research is still being done to determine the best ways to use exercise to treat the condition.

The complex interplay between blood pressure and diabetes has gained substantial attention in the realm of cardiovascular health. Both conditions are independently recognized as major contributors to morbidity and mortality, and their coexistence often leads to a synergistic escalation of cardiovascular risk. Insulin resistance, a hallmark of type 2 diabetes, is closely intertwined with hypertension. Impaired insulin signaling not only contributes to dysregulated glucose metabolism but also impacts vascular function, leading to increased arterial stiffness and elevated blood pressure. Diabetes and hypertension are deeply associated due to similar risk factors, such as endothelial dysfunction and the Renin-Angiotensin-Aldosterone System (RAAS). Diabetes-induced endothelial dysfunction plays a pivotal role in the elevation of blood pressure. It is characterized by reduced nitric oxide bioavailability, increased oxidative stress, and inflammation that contribute to impaired vasodilation, fostering a hypertensive milieu.

**References**

15. *Get active!*. Centers for Disease Control and Prevention (2022)
16. *Get active!*. Centers for Disease Control and Prevention (2022)
term. Dysregulation of the RAAS is a common denominator in both diabetes and hypertension. Hyperglycemia and insulin resistance activate the RAAS\textsuperscript{18}, promoting vasoconstriction, sodium retention, and vascular remodeling, collectively exacerbating blood pressure elevation.\textsuperscript{19}

Moreover, elevated blood pressure perpetuates an inflammatory cascade, fostering a microenvironment conducive to the development of insulin resistance and impaired glucose metabolism. Hypertension also contributes to oxidative stress, which, in turn, exacerbates insulin resistance. Increased production of reactive oxygen species interferes with insulin signaling pathways, amplifying the risk of beta-cell dysfunction and the progression toward diabetes.

Peripheral arterial disease (PAD) is a condition where blood vessels supplying the extremities become narrowed or blocked. PAD primarily results from atherosclerosis, a process where fatty deposits, cholesterol, and other substances accumulate in the arterial walls, forming plaques.\textsuperscript{20} As atherosclerosis progresses, blood vessels narrow, impeding blood flow to the legs and feet. This reduction in blood supply can lead to pain, tissue damage, and impaired wound healing. The hallmark symptom of PAD is claudication, characterized by pain or discomfort in the legs during physical activity, which usually subsides with rest. Peripheral Arterial Disease poses significant challenges to individuals, particularly those with diabetes, highlighting the need for proactive management and preventive measures.

Sleep, a fundamental aspect of human physiology, is now recognized as a modifiable risk factor influencing the development and progression of diabetes. Epidemiological studies consistently associate short sleep duration with an increased risk of developing type 2 diabetes. Sleep deprivation is linked to disruptions in glucose metabolism, insulin resistance, and alterations in appetite-regulating hormones, collectively contributing to an unfavorable metabolic

\textsuperscript{18} The renin angiotensin aldosterone system and insulin resistance in humans. \textit{Current hypertension reports, pg} 59–70.
\textsuperscript{19} Renin-Angiotensin-aldosterone system in diabetes and hypertension. \textit{Journal of clinical hypertension (2011)}
\textsuperscript{20} Prevent diabetes problems: Keep your feet and skin healthy (2000)
Beyond duration, poor sleep quality, characterized by frequent awakenings, sleep fragmentation, and disturbances in sleep architecture, is also implicated in the risk of diabetes. Sleep plays a crucial role in regulating circadian rhythms, influencing the timing of hormonal release and metabolic processes. Disruptions in circadian rhythms, such as those observed in shift work or irregular sleep patterns, can adversely affect insulin sensitivity and glucose homeostasis, leading to insulin resistance and impaired glucose tolerance. Sleep deprivation can alter the balance of appetite-regulating hormones, such as leptin and ghrelin. Reduced sleep is associated with increased ghrelin levels (stimulating appetite) and decreased leptin levels (suppressing appetite), potentially leading to overeating and weight gain, key contributors to insulin resistance and diabetes. Chronic sleep deprivation triggers inflammatory pathways, contributing to a pro-inflammatory state associated with insulin resistance. Elevated levels of inflammatory markers, such as C-reactive protein, may link insufficient sleep to the pathogenesis of diabetes; however, further research is being conducted to confirm this interpretation.

Dietary habits, laden with significance in metabolic regulation, serve as both risk factors and modifiable determinants for diabetes. Diets high in refined carbohydrates and foods with a high glycemic index contribute to rapid spikes in blood glucose levels, promoting insulin resistance over time. Such dietary patterns are associated with an increased risk of type 2 diabetes. The type and quality of dietary fats play a crucial role in diabetes risk. Saturated fats and trans fats are linked to insulin resistance, while polyunsaturated and monounsaturated fats exhibit potential protective effects. Adequate dietary fiber, derived from whole grains, fruits, and vegetables, is inversely associated with diabetes risk. Fiber-rich foods contribute to improved

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21 The epidemiology of sleep and diabetes (2018)
22 The impact of poor sleep on type 2 diabetes (2021)
23 Diabetes and Sleep Disorders (2017)
24 C-reactive protein as a predictor for incident diabetes mellitus among middle-aged men (2003)
glycemic control, enhanced insulin sensitivity, and reduced risk of obesity, offering protective
effects against diabetes. Diets emphasizing whole grains are linked to a lower risk of type 2
diabetes compared to those predominantly composed of refined grains. The complex
carbohydrates and additional nutrients in whole grains contribute to improved insulin function
and metabolic health. Plant-based protein sources, such as legumes and nuts, have been
associated with a lower risk of diabetes. These proteins are often accompanied by dietary fibers
and micronutrients, conferring additional metabolic benefits. On the contrary, diets rich in
processed meats and red meats have been linked to an increased risk of type 2 diabetes. The
presence of saturated fats, heme iron, and other compounds in these meats may contribute to
insulin resistance and inflammation.

In conclusion, the risk factors for diabetes form a complex and interconnected web,
embracing genetic, lifestyle, and environmental influences. The multifactorial nature of
diabetes underscores the importance of a holistic and personalized approach to risk assessment,
prevention, and management. Recognizing the interplay between genetic predispositions and
modifiable lifestyle factors, such as diet, physical activity, and sleep, provides a foundation for
targeted interventions. Moreover, the intricate relationships between comorbidities, such as
hypertension, and their impact on insulin sensitivity contribute to the complexity of diabetes risk.
As our understanding of the molecular and physiological pathways deepens, it becomes
increasingly evident that diabetes is not solely a consequence of isolated factors but rather a
convergence of various elements. Public health initiatives should prioritize comprehensive
strategies that address both individual and population-level risk factors. Education on healthy
lifestyle choices, routine screenings, and early interventions are critical components of effective

26 Diabetes diet: Create your healthy-eating plan (2023)
27 Red meat, dietary heme iron, and risk of type 2 diabetes: the involvement of advanced lipoxidation end products. Advances in nutrition (2013)
diabetes prevention. Furthermore, recognizing the significance of personalized interventions tailored to an individual's genetic makeup, cultural background, and unique metabolic profile will enhance the precision and efficacy of preventive measures. As the global prevalence of diabetes continues to rise, the imperative to mitigate its impact on individuals and healthcare systems alike becomes even more pressing. By fostering a collective commitment to understanding, addressing, and preventing diabetes risk factors, we can aspire to a future where the burden of this chronic condition is significantly reduced, and the pursuit of global metabolic health remains a shared priority.

Diabetes manifests a spectrum of symptoms that can vary in severity and onset, depending on the type of diabetes and individual factors. Recognizing these symptoms is crucial for early detection and timely intervention. The primary symptoms include elevated blood glucose levels and the physiological consequences of insulin deficiency or resistance. Individuals with diabetes often experience an increased frequency of urination, known as polyuria. This results from the kidneys attempting to eliminate excess glucose from the blood, leading to increased urine production. Diabetes-induced polyuria can trigger excessive thirst or polydipsia.\(^\text{28}\) The body attempts to compensate for fluid loss by signaling an increased need for water intake. Despite increased calorie consumption, individuals with diabetes may experience persistent hunger or polyphagia. This paradoxical phenomenon is linked to cellular starvation resulting from inadequate glucose utilization. Unintentional weight loss, despite normal or increased food intake, is a common symptom of diabetes. The body resorts to breaking down muscle and fat for energy due to insufficient glucose utilization. Chronic fatigue and weakness are frequent complaints in individuals with diabetes. The body's inability to utilize glucose

\(^{28}\) *Diabetes Insipidus* (2021)
efficiently can result in reduced energy levels. Fluctuations in blood glucose levels can affect the fluid balance in the eye lens, leading to temporary changes in vision. Impaired wound healing is associated with diabetes, attributed to compromised circulation and the regenerative capacity of tissues. Prolonged hyperglycemia can lead to nerve damage, resulting in numbness, tingling, or pain, particularly in the extremities. Recognizing these symptoms and their interplay is essential for early diagnosis and effective management of diabetes.

Diabetes is often accompanied by a spectrum of lower extremity issues, ranging from neuropathy to vascular complications. These issues pose significant challenges to individuals with diabetes, leading to an increased risk of foot ulcers, infections, and, in severe cases, amputations. Understanding the interplay between diabetes, neuropathy, and vascular problems is crucial for effective prevention and management.

Diabetic peripheral neuropathy impairs autonomic, motor, and sensory functions by altering the normal operations of nerves throughout the body. Chronic hyperglycemia is a primary driver of nerve damage in diabetes. Elevated glucose levels contribute to oxidative stress, inflammation, and microvascular changes, affecting nerve structure and function. Peripheral neuropathy in diabetes encompasses both axonal degeneration and demyelination, disrupting the normal transmission of nerve signals. Peripheral neuropathy was almost twice as prevalent in people with diabetes compared to those without diabetes. There are three clinical manifestations of peripheral neuropathy; they include sensory neuropathy, autonomic neuropathy, and motor neuropathy. Sensory neuropathy includes loss of sensation, tingling, or pain in the extremities. Individuals may experience difficulty detecting temperature changes, injuries, or pressure. Autonomic nerve damage can affect various bodily functions, leading to

29 The current burden of diabetic foot disease. *Journal of clinical orthopedics and trauma* pgs 88–93
30 The diabetic foot: medical and surgical management (2012)
31 The diabetic foot: medical and surgical management (2012)
symptoms such as gastroparesis, orthostatic hypotension, and impaired sweating. Motor neuropathy includes weakened muscles, muscle cramps, and altered gait are indicative of motor neuropathy by unraveling the complicated connections between hyperglycemia, nerve damage, and clinical manifestations, healthcare providers can tailor interventions to alleviate symptoms, slow progression, and enhance the overall well-being of individuals with diabetes. Emphasizing preventive measures, optimal glycemic control, and patient education is pivotal in mitigating the impact of peripheral neuropathy and fostering a higher quality of life for those navigating the intersection of diabetes and neuropathy.

Diabetic foot ulcers represent a serious and challenging complication of diabetes, significantly impacting the health and quality of life of affected individuals. As chronic wounds that often resist conventional healing, diabetic foot ulcers pose a considerable risk of infection, tissue damage, and amputation. Understanding the factors contributing to ulcer development, the intricate relationship with diabetes, and effective management strategies are essential for comprehensive care. Neuropathy may lead to foot deformities and alterations in gait, resulting in increased pressure on specific areas of the foot. Prolonged pressure can cause calluses, which may develop into ulcers. The longer the duration of diabetes and the poorer the glycemic control, the higher the risk of developing foot ulcers. The combination of neuropathy and vascular disease significantly increases susceptibility to ulcer formation, as well as structural abnormalities and trauma coupled with reduced sensation. Diabetic foot ulcers commonly occur on pressure points, such as the sole. They may present as non-healing sores, with or without signs of infection. Left untreated, diabetic foot ulcers can lead to cellulitis, abscess formation, and osteomyelitis (infection of the bone), and may necessitate amputation.

32The diabetic foot: medical and surgical management (2012)
Healthcare workers may diagnose ulcers by thorough examination, including an assessment of sensation, vascular status, and wound characteristics. Imaging studies such as X-rays, MRI, or CT scans may be employed to assess the extent of tissue involvement and identify underlying bone infections. Diabetic patients are often informed of diligent wound care techniques, including cleaning, debridement, and dressing changes. They may even be appointed offloading and pressure redistribution devices, such as special footwear or casts to help reduce pressure on ulcerated areas and facilitate the healing process. Antibiotics may be prescribed to manage or prevent infections, and surgical interventions may be necessary for severe cases. Effective management of diabetic foot ulcers requires a multidisciplinary approach involving endocrinologists, podiatrists, wound care specialists, and vascular surgeons. Diabetic foot ulcers represent a significant clinical challenge, necessitating a comprehensive and collaborative approach to care. By addressing the multifaceted factors contributing to ulcer development, emphasizing preventive measures, and engaging in vigilant wound care, healthcare providers can enhance the quality of life for individuals with diabetes. The integration of patient education, glycemic control, and a multidisciplinary care model is pivotal in navigating the complex intersection of diabetes and foot ulcers, ultimately reducing the risk of complications and improving long-term outcomes.

**Aim 1**

**Introduction**

The Diabetic Foot Consortium conducts primary research concentrating on identifying biological indicators, or "biomarkers," in patients with diabetic foot ulcers that help direct therapy and forecast the ulcer's healing process and risk of recurrence. This will help doctors tailor treatment to specific individuals and provide preventative treatment.
A recent study done through the Consortium was regarding transepidermal water loss (TEWL). It is a measure of the amount of water that passes through the skin from the inside to the outside. In the context of diabetic foot ulcers, TEWL can be a significant factor influencing wound healing and the overall management of these ulcers. Diabetes can lead to alterations in skin structure and function. The skin of individuals with diabetes is often dry and prone to fissures, compromising its natural barrier function. Elevated TEWL in diabetic skin is indicative of impaired barrier function, leading to increased susceptibility to moisture loss. Excessive TEWL from the wound site can contribute to delayed healing. The wound environment needs to be adequately moist for optimal healing, and high TEWL can impede this process by preventing the formation of a protective barrier. High TEWL can result in the dehydration of the wound bed, adversely affecting cell migration, proliferation, and overall tissue repair. Dry and cracked skin, coupled with elevated TEWL, creates an environment conducive to infection. Microorganisms can enter through these compromised barriers, increasing the risk of wound infections.

Researchers discovered that the frequency of wound recurrence was twice as high in those with a high TEWL reading (>30 grams per meter squared per hour), which indicates poor skin barrier function, as opposed to those with a low TEWL reading (<30g.m-2.h-1). Furthermore, there was a strong agreement between the participants' self-reported recurrence and the clinician's assessment of wound recurrence. The results of the study represent a significant step forward in that direction even if TEWL was not confirmed as a biomarker in this investigation. In focusing on the effect of TEWL on the occurrence of ulcers I wish to expand on the factors affecting TEWL, such as eczema, which is known to increase TEWL. My primary purpose is to observe the effect of eczema on foot ulcer recurrence in diabetic patients.

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33 Defective closure of diabetic foot ulcers is associated with higher risk of wound recurrence (2023)
Methods

Trans-epidermal water loss (TEWL) will be measured on the closed wound site and at a location similar to the wound site (reference site) using a VapoMeter, which is a small wireless probe-like instrument. There will be 200 patients in each patient group. To be eligible to participate in this study, participants should be at least 18 years old, willing and able to comply with protocol instructions, provide written informed consent, and have a clinically diagnosed diabetic foot ulcer (DFU) that is closed. There will be an added criterion of experiencing eczema for patient group 2. Participants will be enrolled within two weeks after the closure of their DFU. Complete wound healing will be verified at a second visit two weeks later and this visit will start the 16-week timeline where participants will be followed weekly by phone until the earliest of DFU wound recurrence or 16 weeks. Participants who experience a DFU wound recurrence and a subset of participants who do not experience a DFU wound recurrence by week 16 will be asked to attend one final visit.

Possible Results

Eczema is characterized by a compromised skin barrier, leading to increased TEWL. Measuring TEWL in patients with eczema may reveal elevated levels, signifying impaired barrier function. The elevated TEWL in eczematous skin makes it more susceptible to dryness and cracking. This increases the risk of developing fissures, which can serve as entry points for pathogens and contribute to the recurrence of diabetic foot ulcers. In individuals without eczema, TEWL levels may vary based on factors such as overall skin health, hydration status, and environmental conditions. Generally, lower TEWL levels in individuals without eczema suggest intact skin barrier function. However, variations can still occur based on factors like age, genetics, and skincare practices.

34 TEWL biomarker study for diabetic foot ulcer recurrence (2023)
If TEWL measurements yield insignificant results in both patients with and without eczema in the context of the recurrence of diabetic foot ulcers, it may suggest that, at least in this specific study or context, TEWL alone may not be a significant predictive factor for ulcer recurrence. The lack of significance in TEWL measurements could emphasize the importance of a comprehensive assessment that includes various clinical parameters. Factors such as the overall health of the skin, the presence of infections, and adherence to foot care protocols should be considered. TEWL can vary widely among individuals, even within the same group. Some patients may have naturally higher TEWL without experiencing adverse outcomes, emphasizing the need to consider individual variability. The timing of TEWL measurements concerning the healing process of foot ulcers may influence results. TEWL, while reflective of skin barrier function, may not capture all aspects of skin health and resilience. Other factors, such as skin hydration, microbial load, and local inflammation, also contribute to the overall condition of the skin. Insignificant results in a single measurement may not rule out the potential relevance of TEWL over time. Longitudinal studies with repeated measurements could provide a more nuanced understanding of its role in diabetic foot ulcer recurrence.

![Normalized TEWL Levels Compared to DFU TEWL Levels in Patients with Eczema](image)

Figure 1: An example of what the collected results (TEWL measurements) would look like at the end of the experiment. A T-test analysis will be performed to determine significance.
Aim 2

Introduction

The human skin, a complex and dynamic organ, hosts a diverse community of microorganisms collectively known as the skin microbiome. This intricate ecosystem plays a pivotal role in maintaining skin health, immune function, and protection against pathogenic invaders. Understanding the composition and dynamics of the skin microbiome is crucial for unraveling its influence on various dermatological conditions, such as eczema and diabetic foot ulcers. In this context, we explore the microbiome of individuals with eczema, as well as the distinct microbial profiles present in the wound ulcers of diabetic patients, with and without coexisting eczema.

The skin microbiome encompasses a plethora of bacteria, fungi, viruses, and other microorganisms that form a symbiotic relationship with the host. These microorganisms contribute to the maintenance of skin homeostasis by preventing the colonization of harmful pathogens, modulating the immune response, and participating in various metabolic processes. The composition of the skin microbiome can vary across different body sites and is influenced by factors such as genetics, environment, and individual hygiene practices.

Eczema, a chronic inflammatory skin condition, has been associated with alterations in the skin microbiome. The disrupted barrier function and immune dysregulation characteristic of eczema create an environment conducive to shifts in microbial communities. Previous studies have indicated variations in the abundance and diversity of certain bacterial species in the skin microbiome of individuals with eczema compared to those with healthy skin.

Diabetic foot ulcers, a serious complication of diabetes, present a unique challenge in wound management. Adding another layer of complexity, the coexistence of eczema in diabetic
patients may further impact the microbiome of foot ulcers. The altered skin environment, impaired circulation, and compromised immune function in diabetes contribute to the development of chronic wounds. Investigating the microbiome of wound ulcers in diabetic patients, with and without eczema, can unveil potential microbial signatures associated with these conditions.

Methods

Participants will be divided into two groups: those with diagnosed eczema (Group A) and those without eczema (Group B). Informed consent will be obtained from each participant. Sterile swabs will be used to collect samples from the borders and base of foot ulcers. Samples will be streaked on growth media for bacterial isolation. We will use a MacConkey agar plate for the growth of gram-negative bacteria and Mannitol Salt agar plates for gram-positive bacteria. Identification of bacterial species will be performed using standard microbiological techniques, such as a T streak or Four Quadrant streak procedure. The antibiotic susceptibility of isolated bacteria will be determined using the Kirby-Bauer disk diffusion method. A panel of clinically relevant antibiotics, including cilastatin, ciprofloxacin, ceftazidime, and dicloxacillin will be selected. These are known agents taken to treat DFUs. Zones of inhibition will be measured and interpreted according to established guidelines. Statistical analysis, such as ANOVA will be conducted to compare the prevalence and diversity of bacteria between Group A and Group B. The antibiotic resistance patterns will be analyzed to identify any significant differences or trends.

Possible Results

The analysis of microbial composition in diabetic foot ulcers may reveal a diverse array of bacteria, including species commonly associated with skin infections. Staphylococcus aureus,
Streptococcus spp., and Enterococcus spp. are likely to be prevalent, reflecting the typical microbiota found in chronic wounds. Diabetic patients without eczema may display a relatively balanced and diverse microbial community in foot ulcers. In contrast, individuals with both diabetes and eczema may exhibit altered microbial diversity, potentially with a higher prevalence of pathogenic species. Staphylococcus aureus and Staphylococcus epidermis may be more abundant in diabetic patients with eczema due to the skin barrier compromise associated with eczematous conditions.

Diabetic foot ulcers in patients with eczema may exhibit higher levels of antibiotic resistance compared to those without eczema. Commonly used antibiotics, such as beta-lactams and fluoroquinolones, may show reduced efficacy against the isolated bacterial strains in patients with both diabetes and eczema. Increased resistance to commonly prescribed antibiotics for wound infections, such as clindamycin or ciprofloxacin, may be observed in both groups, but potentially more pronounced in the presence of eczema. The purpose of this study is to determine the most effective antibiotic and change treatment procedure if the results are significant for the antibiotic sensitivity of eczema-related DFU bacteria.

**Conclusion**

This data could have great clinical implications for DFU prevention. For patients with eczema or elevated TEWL, targeted interventions such as emollient use and barrier creams become crucial. These measures aim to restore skin barrier integrity and reduce the risk of skin breakdown. Routine TEWL measurements, especially in patients with a history of diabetic foot ulcers, can aid in the early detection of potential issues. Regular monitoring allows for proactive intervention and preventive measures. Patients with eczema should be advised to avoid irritants that can exacerbate skin dryness and inflammation. Tailoring care plans based on individual
TEWL measurements and skin conditions can enhance the effectiveness of preventive strategies. A multidisciplinary approach involving dermatologists, podiatrists, and endocrinologists is crucial. Coordinated efforts address both skin conditions like eczema and systemic factors contributing to diabetic foot ulcers.

The investigation into the microbial composition of foot ulcers in diabetic patients, with and without coexisting eczema, alongside the assessment of antibiotic resistance, will provide valuable insights into the intricate interplay between skin conditions, diabetes, and microbial dynamics. The results may significantly contribute to our understanding of the complexities associated with diabetic foot complications and have implications for the development of targeted therapeutic interventions. Key findings include variations in microbial diversity, abundance of specific bacterial species, and notable differences in antibiotic resistance patterns between diabetic patients with and without eczema. The observed differences in microbial composition and antibiotic resistance profiles suggest the need for refined treatment strategies tailored to the specific conditions of diabetic patients with eczema. Personalized therapeutic approaches, considering the unique microbial landscape, could enhance treatment efficacy and reduce the risk of antibiotic resistance. The identified microbial signatures associated with diabetic foot ulcers, particularly in the presence of eczema, may serve as potential biomarkers for predicting the progression and severity of skin complications. Such biomarkers could aid clinicians in early intervention and more targeted management. The study results could inform wound care practices, guiding healthcare professionals in selecting appropriate antimicrobial agents for diabetic foot ulcers based on the identified microbial composition. This knowledge may contribute to more effective wound management and improved patient outcomes.
These methods can assist medical professionals in estimating the chance that a diabetic foot ulcer will reopen in the future, according to the findings of this study. There may be tens of millions of Americans who have diabetes and could avoid undergoing amputations due to this research and preventative measures.36

36 Defective closure of diabetic foot ulcers is associated with higher risk of wound recurrence (2023)
Bibliography


among older adults. JAMA network open.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9526092/

Defective closure of diabetic foot ulcers is associated with higher risk of wound recurrence.
Indiana University School of Medicine. (2023, June 26).

https://doi.org/10.1016/j.jcot.2021.01.017


https://www.hopkinsmedicine.org/health/conditions-and-diseases/diabetes/gestational-diabetes#:~:text=Age%20(women%20who%20are%20older,known%20as%20impaired%20glucose%20tolerance

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4038351/


https://bio.libretexts.org/Bookshelves/Microbiology/Microbiology_(Boundless)/06%3A_Culturing_Microorganisms/6.03%3A_Culturing_Bacteria/6.3C%3A_Selective_and_Differential_Media


diabetes, multifactorial, gene markers have been confirmed.


