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# Identifying Risk Factors Contributing to Lower Limb Amputations (LLAs) in Diabetic Patients

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The incidence of lower limb amputations (LLAs) linked to diabetes is significantly increasing globally, presenting a major public health concern. This issue is notably acute in Saudi Arabia, where diabetes prevalence has sharply risen. The review aims to investigate the risk factors for LLAs in diabetic patients, focusing on demographic variables, body weight, smoking status, concurrent medical conditions, and laboratory findings. The review was based on English language, peer-reviewed studies published from 2018 to 2023 in medical and human health research. From 53 studies meeting the inclusion criteria, four themes emerged: Global Burden of Diabetes Mellitus, Types and Complications of Diabetes Mellitus, LLAs, and Risk Factors for LLAs in Diabetic Patients. The review concluded that LLAs in diabetic patients are influenced by demographic and disease-specific variables, lifestyle choices, and diabetic complications. The findings underscore the need for risk consideration, particularly in patients with a history of foot ulcers or previous amputations, to develop effective interventions mitigating LLA risks in diabetics. The review is particularly relevant to the context of Saudi Arabia.

**Keywords: Diabetes, Lower Limb Amputation, Risk Factors, Saudi Arabia, Peripheral neuropathy, Peripheral arterial disease, Foot ulcers**

## INTRODUCTION

**D**iabetes mellitus (DM) is an urgent global health concern affecting individuals across all socioeconomic strata and geographic locales, from urban to rural areas, in both developed and emerging economies (Oguntibeju, 2019). Amplified by the escalating obesity epidemic, DM has risen as one of the foremost health issues of the current era, ranking as the seventh leading cause of death worldwide. DM detrimentally affects a person's functional capabilities and life quality, enhancing morbidity rates and hastening mortality(Khan et al., 2020). Despite these alarming circumstances, DM prevalence continues to surge globally, with projections of reaching 700 million affected individuals by 2045 (Saeedi et al., 2019).

Type 2 diabetes accounts for 90-95% of global diabetes cases (Natorska, 2021; Siedlecki et al., 2019). Alarmingly, over 120 million people in Southeast Asia and the Western Pacific remain oblivious to their DM status due to factors such as healthcare accessibility and asymptomatic progression. This lack of diagnosis is notably prevalent among these regions, affecting approximately 193 million people globally. As of recent figures, Africa, Europe, the Middle East and North Africa, North America and the Caribbean, South and Central America, Southeast Asia, and the Western Pacific reported 16, 58, 39 (10.8%), 46 (11%), 26 (9.6%), 82 (19.3%), and 159 (37.4%) million affected individuals respectively(Glovaci et al., 2019).

Saudi Arabia is a striking case study, being one of the countries with the highest DM prevalence and incidence rates. Over recent years, the nation has witnessed a significant escalation in DM incidence (7). Ranked sixth globally for DM prevalence, Saudi Arabia exhibits a 20.0% prevalence rate among individuals aged 20 to 79, with forecasts suggesting either a maintenance or elevation of this ranking in the future(Fawzy et al., 2019). The International Diabetes Federation (IDF) warns that by 2030, if preventative measures are not implemented, half of Saudi Arabia's population will suffer from DM(Hazari & Maiya, 2020).

Globally, type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM) are the most common forms of diabetes, with T2DM representing around 90% of all cases. Other less prevalent types include monogenic diabetes and cystic fibrosis-related diabetes (CFRD)(Zhang et al., 2020).

Regardless of diabetes type, potential complications include microvascular and macrovascular disorders such

as nephropathy, retinopathy, neuropathy, atherosclerotic cardiovascular disease, and heart failure. These complications exacerbate with the severity and duration of poorly controlled diabetes, especially when accompanied by other comorbidities such as dyslipidemia and hypertension. Furthermore, diabetes is a leading cause of blindness due to retinopathy, accounting for 12,000 to 25,000 new cases annually. Renal dysfunction is another significant source of morbidity and mortality in diabetic patients(Sapra et al., 2023).

DM is also the leading cause of limb amputations due to its implications on vasculopathy and neuropathy(Sapra et al., 2023). Diabetic neuropathy, a long-term diabetes complication, typically develops slowly, potentially over decades. An estimated 50% of diabetic patients suffer from neuropathy; 34% will experience a foot ulcer, half of which will become septic; and 20% will necessitate LLA (Zhang et al., 2020). In Saudi Arabia, 15–25% of diabetic foot ulcer cases result in foot amputations. An estimated 15% of Saudi diabetics are projected to develop these ulcers in their lifetimes(Fawzy et al., 2019), with anticipations of half a million annual LLAs due to diabetes within the next decade (Alkenani et al., 2021).

LLAs, defined as the surgical removal of bones and soft tissues in the lower leg, can occur at multiple levels, including the foot or toes, ankle, below or above the knee, or even at the hip joint(Alkenani et al., 2021; Rathnayake et al., 2020). Numerous risk factors contribute to the incidence of LLAs in diabetic patients, such as demographic elements (age and gender) and comorbidities like peripheral vascular disease, neuropathy, renal disorders, osteomyelitis, and diabetic foot ulcers (Sapra et al., 2023; Zhang et al., 2020).

**Significance of study**

The significance of this review lies in its profound investigation into the complex risk factors leading to LLAs among diabetic patients. Despite the development of multidisciplinary amputation prevention teams, one lower limb is lost every 20 seconds globally due to diabetes complications(Edmonds et al., 2021). These LLAs cause life-altering impacts, affecting patients functionally, psychologically, socially, and economically(Cornell & Meyr, 2018).

Over the past half-decade, diabetes mellitus has raised the likelihood of LLAs by up to 56%, with around 85% of such amputations linked to a poorly healing ulcer (Musa et al., 2018). Given the rapid surge in diabetes and diabetic foot ulcers worldwide, diabetes-related LLAs are expected to remain a major cause of morbidity and mortality(Sarfo-Kantanka et al., 2019).

The economic impact of LLAs is also substantial. Treating a simple diabetic foot ulcer can cost around $16,000, which can rise to $30,000 in cases requiring a major amputation (Alshammary et al., 2020). In 2016, the Saudi population afflicted with diabetes reached 4.6 million, projected to nearly double to 8.4 million by 2030(Alasiri & Mohammed, 2022; Jadwa Investment, 2021). Consequently, there is a pressing need to implement corrective strategies emphasizing preventive health measures. Approximately 90,000 citizens succumb annually to premature deaths from chronic diseases, resulting in a life expectancy of 5.2 years lower than the global average (MOH, 2023). As such, preventive healthcare must encompass many conditions, including heart disease, stroke, diabetes, respiratory diseases, mental health, congenital diseases, and traffic accidents.

Saudi Arabia is confronting a substantial increase in diabetes, leading to a rise in LLAs. This alarming trend poses a significant hurdle to realizing Saudi Arabia's Vision 2030, which underlines creating a thriving society with healthful citizens. Furthermore, the economic burden LLAs impose on the healthcare system concerns the nation's sustainable economic development, a pivotal component of Vision 2030 (Alasiri & Mohammed, 2022; Jadwa Investment, 2021; MOH, 2023). Through the targeted management of these risk factors, LLA prevention can contribute towards healthcare expenditure optimization, directly facilitating the country's economic sustainability objectives. Overall, this study significantly bolsters Saudi Arabia's efforts in achieving its Vision 2030 targets, thereby fortifying the nation's health sector and economic resilience.

**Significance of the review**

This review findings provide critical insights that enable healthcare authorities in Saudi Arabia to tailor their strategies for diabetes management, thereby aligning with Vision 2030's goals more effectively. By comprehending the intricate factors precipitating LLAs, such as demographic factors, body weight, smoking habits, co-existing medical conditions, and laboratory findings, these authorities can formulate more potent preventive measures and treatment protocols for diabetic patients.

Therefore, carries significant implications for Saudi Arabia, where diabetes prevalence is increasing sharply. It can guide healthcare professionals, policymakers, and researchers in developing effective interventions and shaping policies that address these risk factors, ultimately reducing the incidence of LLAs among diabetics. Additionally, this review may contribute to the existing literature on the risk factors for LLA among diabetic patients, especially in the Saudi Arabian context.

**Purpose of Review**

The aim of this literature review is to delve into the risk factors for LLA among diabetic patients, with a specific focus on demographic variables, body weight, smoking status, concurrent medical conditions, and

relevant laboratory findings.

**PICOT question**

**Population:** Diabetic Patients

**Intervention:** Identification of risk factors

**Outcome:** Lower Limb Amputations (LLA)

**Time:** Studies published from 2018 to 2023

"In diabetic patients (Population), how do factors such as demographics, body weight, smoking status, comorbidities, and laboratory findings (Interest/intervention) contribute to the incidence of lower limb amputations (Outcome) in studies published from 2018 to 2023 (Time)?"

**Search Strategy:**

The scope of this review was determined by the inclusion criteria, covering studies that precisely addressed and scrutinized the risk factors for LLAs among diabetic patients. The focus areas of these studies encompassed demographic characteristics, body weight and smoking status, concurrent medical conditions, and pertinent laboratory investigations.

**Key Search Terms**

The initial search used the following keywords : Risk Factors: risk factors, contributing factors, predictors, determinants. Lower Limb Amputation: lower limb amputation, major amputation, lower extremity amputation, LLA. Patients with Diabetes: diabetes patients, individuals with diabetes, diabetic population. Saudi Arabia: Saudi Arabia, Kingdom of Saudi Arabia, KSA. Diabetes Mellitus: diabetes mellitus, type 2 diabetes, type 1 diabetes. Also, the Boolean connectors were as follows: "Risk Factors" AND "Lower Limb Amputation" AND ("Patients with Diabetes" OR "Diabetes Mellitus"), "Saudi Arabia" AND ("Lower Limb Amputation" OR "Patients with Diabetes"), "Worldwide" AND ("Risk Factors" OR "Lower Limb Amputation" OR "Patients with Diabetes" OR "Diabetes Mellitus").

**Inclusion Criteria**

The inclusion criteria dictated the selection of records that addressed the research questions on the risk factors for LLA among patients with diabetes. Included studies that had full access and were conducted in the setting of medical publications and the human field. The study included peer-reviewed studies published in English and within the last five years (2018-2022).

**Exclusion Criteria**

To maintain focus and relevance to the research question, certain studies were deliberately excluded from the literature review. These exclusion criteria were defined based on factors including patient age, relevance to the analysis, study design, and language. Studies that focused primarily on younger patients were not considered for this review as they did not provide relevant information about the risk factors for LLA among patients with diabetes, which is more prevalent in older patients. Additionally, studies that contained irrelevant data for analysis were also excluded. The emphasis of this review is on studies that offer data directly related to the risk factors for LLA among patients with diabetes; therefore, any studies that were determined as unrelated to this specific research inquiry were not included.

**Search Strategy:**

The scope of this review was determined by the inclusion criteria, covering studies that precisely addressed and scrutinized the risk factors for LLAs among diabetic patients. The focus areas of these studies encompassed demographic characteristics, body weight and smoking status, concurrent medical conditions, and pertinent laboratory investigations.

**Study Selection Process**

The selection process utilized PRISMA 2020 Flow Diagram, as shown in Figure 1. The primary purpose of PRISMA is to facilitate the screening and selecting of the studies for the literature review. The flow diagram improved the transparency of the evaluation and subsequent discussion. However, three phases were applied to reach the final step in the PRISMA diagram, including the identification phase, screening phase, and included studies phase. More than thousands of studies were determined in the initial search. In the identification phase, the total number of studies generated from PubMed, MEDLINE, Google Scholar, Science Direct, and CINAHL was 1453. Of 1453, 711 were removed due to duplication. In the screening phase, 454 studies were excluded, and 230 studies were not retrieved due to not matching the inclusion criteria of the present study. In the last phase, the remaining 68 reports were considered for quality synthesis but led to further removal based on age (n = 5), Relevance (n = 3), design (n = 3), and language (n = 4). Consequently, the screening generated 53 studies, which informed the literature review's quality synthesis and critical analysis.

The final 53 studies chosen to fulfil the inclusion criteria were also relevant to the PIO question. The researcher relied on the research questions to include and exclude studies, and Key search words and synonyms were created from the research question.

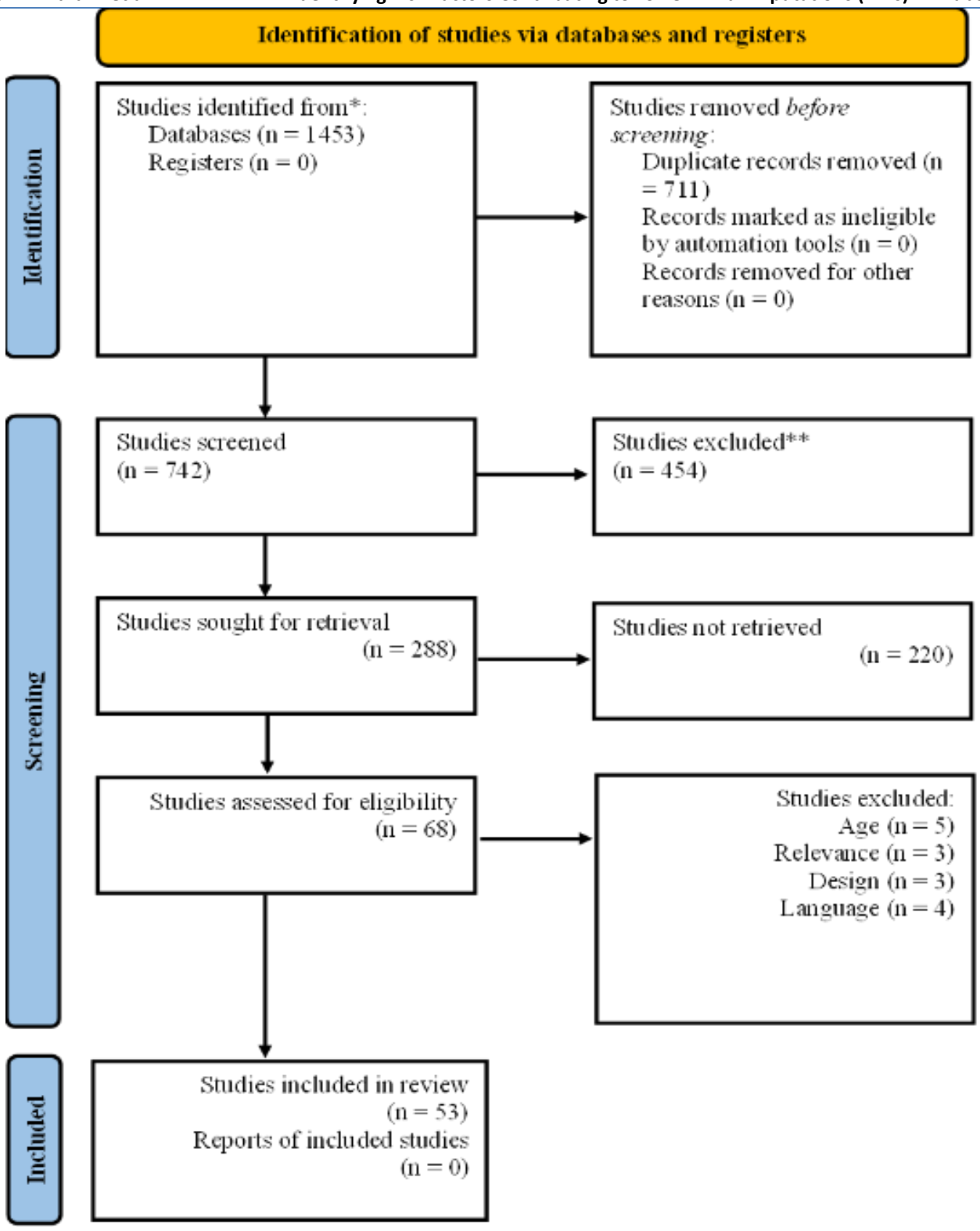


**Figure 1: The PRISMA diagram describes the decision-making process researcher used during the overview**

**Figure 1** presents The PRISMA flow diagram used to report the studies' screening, and this diagram lists all the choices made during the research selection process. The literature utilized in this review is sourced from various countries, providing a comprehensive global perspective on the available evidence. However, in this study, four primary themes emerged from the literature. These themes include:

1. Global Burden of Diabetes Mellitus: This theme investigates the worldwide impact of Diabetes Mellitus, considering its prevalence, mortality rates, and burden on healthcare systems across different countries.

2. Types and Complications of Diabetes Mellitus: This theme delves into the various types of diabetes Mellitus and the associated complications.

3. Lower Limb Amputation: Under this theme, the focus is on the incidence of LLAs, exploring its occurrence, the procedures involved, and its subsequent impact on a patient's quality of life.

4. Risk Factors for LLA among Diabetic Patients: This theme outlines the various risk factors associated with LLA in patients with diabetes, enabling a comprehensive understanding of the preventable and non-preventable factors.

These themes offer an organized structure for understanding the complexities of Diabetes Mellitus and its association with LLAs.

## Findings

Global Burden of Diabetes Mellitus: Diabetes mellitus is a global public health issue that affects people of all socioeconomic statuses, including those who are educated and those who are not, as well as those who live in urban and rural areas of established and developing nations (Oguntibeju, 2019). Along with the growing obesity crisis, diabetes mellitus has emerged as one of the most important and widespread problems in recent years and is currently the seventh leading cause of mortality globally. Diabetes has a negative impact on a person's functional abilities and quality of life, which increases morbidity and causes early death (Khan et al., 2020).

However, the prevalence of DM is continuously rising globally, and it is predicted that there will be 700 million diabetic patient by year 2045 (Saeedi et al., 2019). Type 2 diabetes accounts for 90-95 precent of all diabetes cases worldwide (Natorska, 2021; Siedlecki et al., 2019).

In addition over 120 million people in Southeast Asia and the Western Pacific are unaware that they have diabetes mellitus because of variables like access to healthcare and quiet development with few symptoms and indicators. Despite this worrisome prevalence of DM, there is still a lack of diagnosis impacting about 193 million people globally, with the biggest proportion being in these regions. There were 16 million people with diabetes in Africa, 58 million in Europe, 39 million (10.8%) in the Middle East and North Africa, 46 million (11%) in North America and the Caribbean, 26 million (9.6%) in South and Central America, 82 million (19.3% of the total in the world) in Southeast Asia, and 159 million (37.4% of the total in the world) in the Western Pacific (Glovaci et al., 2019).

Saudi Arabia considered one of the highest prevalence and incidence rates of diabetes in the world. The extent of diabetes' pervasiveness in this nation has likewise dramatically expanded over the past few years (Robert & Al Dawish, 2020). As one of the top ten countries for diabetes prevalence (ranked sixth in the world), Saudi Arabia is predicted to retain its present prevalence rate of 20.0% among individuals aged 20 to 79 and either exceed or retain this rank in the coming years (Fawzy et al., 2019). The International Diabetes Federation (IDF) made a scary prediction that by 2030, half of Saudi Arabia's population will have diabetes if nothing is done to stop it (Hazari & Maiya, 2020).

### Types and Complications of Diabetes Mellitus:

The review highlights the three most prevalent forms of diabetes worldwide, namely type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM). T2DM accounts for approximately 90% of all diabetes cases, while T1DM and GDM constitute the remaining cases (Zhang et al., 2020).

The review emphasizes that poorly controlled diabetes, regardless of its specific type, can lead to various microvascular and macrovascular complications. These complications include nephropathy, retinopathy, neuropathy, atherosclerotic cardiovascular disease, and heart failure events. The severity and duration of uncontrolled diabetes, along with comorbidities such as dyslipidemia and hypertension, influence the development and progression of these complications (11).

One of the significant complications associated with diabetes is blindness caused by retinopathy. Each year, retinopathy contributes to a considerable number of new cases of blindness, ranging from 12,000 to 25,000. Renal dysfunction is another prevalent complication leading to morbidity and mortality among individuals with diabetes. Furthermore, diabetes mellitus is a major cause of LLAs, primarily attributable to the vasculopathy and neuropathy it induces(Sapra et al., 2023) .

Diabetic neuropathy, a long-term complication of diabetes, typically manifests gradually over several decades. The review reports that up to 50% of diabetic patients are estimated to develop neuropathy, and around 34% may experience a foot ulcer at some point in their lives. Alarmingly, half of these ulcers may become septic, and ultimately, approximately 20% of individuals will require LLA (Zhang et al., 2020).

The findings of this systematic review underscore

the importance of early and effective management of diabetes to prevent or minimize its complications. The high prevalence of T2DM and its associated complications necessitate comprehensive strategies for prevention, early detection, and treatment. Timely interventions, including proper glycemic control, regular screening for complications, and lifestyle modifications, can significantly reduce the burden of diabetes-related complications and improve the quality of life for individuals living with diabetes.

**Lower Limb Amputation:**

LLA is a significant concern in Saudi Arabia, particularly in relation to diabetic foot ulcers. The prevalence of foot amputations in cases of diabetic foot ulcers is estimated to be between 15% and 25%(Fawzy et al., 2019). The high incidence of diabetic foot ulcers among Saudi diabetics, with 15% predicted to develop ulcers throughout their lifetimes, highlights the severity of the problem (Fawzy et al., 2019). Alarming projections indicate that within the next decade, Saudi Arabia may witness approximately half a million LLAs annually as a result of diabetes (Alkenani et al., 2021).

LLA involves the surgical removal of bones and soft tissues at various levels of the lower leg. Minor amputations typically occur below the ankle joint and involve the toe and forefoot, while major amputations occur at or near the ankle joint, including those below or above the knee(Rathnayake et al., 2020). Studies indicate that LLAs can occur at different levels, such as the foot, toes, ankle, below the knee, at the knee, above the knee, and even at the hip(Boyko et al., 2018; Gurney et al., 2018; Shatnawi et al., 2018).

Above-knee amputation (AKA), also known as transfemoral amputation, involves the removal of the thigh bone above the knee joint. This procedure is necessary in cases where conditions like infection or vascular impairment are present(Myers & Chauvin, 2023; Trouillez et al., 2021). Hemipelvic amputation, also referred to as transpelvic amputation, involves the removal of a portion of the pelvis and the hip joint. This complex procedure requires the use of a prosthetic device to support walking due to the absence of a residual limb(Azar & Beaty, 2021). Hip disarticulation (HD) is a severe form of LLAs, performed by severing the leg at the hip joint. It is considered a last resort under critical circumstances, typically for conditions such as necrotizing fasciitis, severe infection, trauma, ischemia, or malignancy(Simman et al., 2022).

Below-knee amputation (BKA), or transtibial amputation, involves the removal of the foot, ankle joint, distal tibia, fibula, and associated soft tissues. BKA is the most common type of amputation performed and carries a lower risk of post-operative complications compared to transfemoral amputation (Adams & Lakra, 2023; Guest et al., 2019). Partial foot amputation, also known as transmetatarsal amputation (TMA), involves the removal of the toes and a portion of the foot's long bones. This procedure is often used to treat foot gangrene and infection while preserving functional mobility (Aljarrah et al., 2022; Harris & Fang, 2021).

Toe amputations are primarily performed due to low blood supply leading to gangrene, which is a common complication among diabetic patients. Physical therapy may be occasionally employed to address balance or gait issues following this type of amputation (Al Wahbi, 2018; van Netten et al., 2020).

The discussion highlights the different levels and types of LLAs, reflecting the severity and diversity of cases encountered in Saudi Arabia. Understanding the specific procedures and indications for each type of amputation is crucial for healthcare professionals involved in managing diabetic foot ulcers and other conditions that may lead to the need for amputation. Further research and interventions are needed to address the rising prevalence of LLAs and to develop strategies for prevention, early detection, and effective management of diabetic foot ulcers in Saudi Arabia.

**Risk Factors for Lower Limb Amputation among Diabetic Patients:**

The implications of amputation on an individual's economic, psychological, and social well-being are substantial and long-lasting (Shahine et al., 2022). Moreover, the global prevalence of amputations has been increasing, with diabetic complications accounting for 40% to 60% of nontraumatic LLAs worldwide, and 80% of these cases being preceded by diabetic foot ulcers(Lin et al., 2020).

To comprehensively identify the factors that predict the risk of LLA, we conducted a thorough review of the literature, incorporating data from various sources. The literature reveals that a multitude of factors influence the likelihood of LLA among diabetic patients. These factors encompass socio-demographic characteristics, genetic features, duration of illness, unhealthy habits, hyperglycemia, and diabetic comorbidity.

**Demographic risk factors for LLA:** Evidence indicates that older age and male gender contribute to elevated LLA risk in diabetic patients. Boyko et al., (2018) found in a 22-year prospective US study of 1,461 male patients, that being over 70 significantly increased LLA risk(Boyko et al., 2018). This finding is supported by a Saudi Arabian study by Musa et al., (2018) and a Brazilian study by Alves and Laporta (2020), both of which identified older age as a risk factor(Alves & Laporta, 2020; Musa et al., 2018). The latter also noted the predominance of males among amputees, a trend consistent across ethnicities and geographic locations(Alves & Laporta, 2020), potentially attributable to higher rates of severe peripheral artery disease, smoking, and road traffic accidents among males (Shahine et al., 2022).

These findings are corroborated by two systematic

reviews and meta-analyses by Rodrigues et al., (2022) and Bandarian et al., (2022) which identified age and male gender as major risk factors(Bandarian et al., 2022). Further backing these findings, a Saudi Arabian retrospective study by Shahine et al., (2022) found that the elderly have a 10%–15% lifetime amputation risk, 10–30 times higher than the general population, with males dominating the amputee group(Shahine et al., 2022). Similar results were reported by Hallström et al., (2021) in a Swedish study focusing on type 1 diabetes(Hallström et al., 2021).

However, pain response varies by gender, with men exhibiting higher sensitivity, but women facing more painful diseases overall. Social and familial obligations might cause men to dismiss minor foot lesion changes, delaying the detection of severe foot ulcers (Benavent et al., 2020; Lin et al., 2020).

LLA incidence is higher among individuals with limited formal education, low socioeconomic status, long-standing diabetes, and those who are unmarried, divorced, or widowed. These findings underscore the significant role family plays in aiding diabetic patients in foot care, particularly when complicating factors exist (Benavent et al., 2020; Harding, 2020).

Functional mobility also plays a role, with improved circulation and vascular supply due to increased movement believed to decrease LLA risk (Clement et al., 2019; Lin et al., 2020).

The duration of diabetes correlates with an increased likelihood of LLA. Ying et al., (2022) demonstrated in a Singaporean cohort study that patients with diabetes for 15 years or more had a 23-fold increased LLA risk(Ying et al., 2022). This was supported by Rodrigues et al., (2022), Shatnawi et al., (2018), and Prakash et al.,( 2019), who noted the enhanced risk among patients with a longer history of diabetes and among certain ethnic groups(Prakash et al., 2019; Rodrigues et al., 2022; Shatnawi et al., 2018).

Several studies, identified that certain abnormal laboratory results were associated with a higher risk of amputation such as, the poor glycemic control reflected in high levels of HbA1c were associated with higher incidence of LLA among diabetic patients (Almohammadi et al., 2021; Bandarian et al., 2022; Guo et al., 2019; Li et al., 2020; Prakash et al., 2019; Sadriwala et al., 2018; Shatnawi et al., 2018). Also, the literature agreed on that the high white blood cell count (WBC) were factors associated with amputation among diabetic patents (Almohammadi et al., 2021; Lin et al., 2020; Musa et al., 2018).

**Body weight and smoking**Recent research indicates that an increase in body weight and smoking habits can significantly contribute to these risks. Specifically, an increase in body mass index (BMI), particularly values exceeding 32 kg/m2, has been linked to an increased risk of DFUs as per a 2022 study by Al-Mohaithef et al., conducted in Egypt(Al-Mohaithef et al., 2022). A similar correlation was observed in the United States, where Boyko et al., (2018) found that each 21.4-kg increase in body weight was associated with an increased risk of amputation among diabetic patients(Boyko et al., 2018). On the contrary, a meta-analysis by Lin et al., (2020) pointed out that a lower BMI, rather than higher, was associated with an increased risk of amputation(Lin et al., 2020).

Turning to smoking, patient behaviors like tobacco usage significantly contribute to an increased rate of amputations. The meta-analysis by Lin et al., (2020) and a systematic review by Rodrigues et al., (2022), found that a patient's smoking history significantly increased their risk for amputation(Lin et al., 2020; Rodrigues et al., 2022). The findings were further reinforced by studies conducted by Ying et al., (2022) in Singapore(Ying et al., 2022), Ha Van et al., (2020) in France(Fox et al., 2022), Al-Mohaithef et al., (2022) in Egypt(Al-Mohaithef et al., 2022), Alkenani et al., (2021) in Saudi Arabia(Alkenani et al., 2021), Prakash et al., (2019) in India(Prakash et al., 2019), and Hallström et al., (2021) in Sweden (Hallström et al., 2021).

It is noteworthy that nicotine, a key component of tobacco, induces the heart to beat approximately 20 beats faster per minute for each cigarette consumed. This increased heart rate, coupled with its vasoconstrictive effects, causes arterial contraction throughout the body. As nicotine accelerates arterial hardening and constriction, this can lead to ischemia and potentially result in LLA (Hinkle & Cheever, 2018; Stromberg & DeWit, 2023).

**Comorbidities in the Diabetic Patient as Risk Factors for LLA:** Li et al.'s (2020) Taiwanese retrospective population-based cohort study aimed to create a reliable LLA risk score system for patients with type 2 diabetes. The study recognized comorbidities and medication usage as predictors for LLA amongst 504 patients.

**Cardiovascular Diseases:** Various international studies have highlighted heart diseases as potential LLA risk factors. For instance, the Systematic Review and Meta-Analysis by Bandarian et al., (2022) underlined peripheral arterial disease and ischemic heart disease as significant DF amputation risk factors. Similar outcomes were noted by Hallström et al., (2021) in Sweden, and Alves and Laporta, (2020) in Brazil, where cardiovascular comorbidities were associated with LLA among diabetic patients. Also, studies from Jordan and India by Shatnawi et al., (2018), and Prakash et al., (2019) respectively, found significant associations between hypertension, cardiac diseases, stroke, and increased LLA incidents. Additionally, studies by Alkenani et al., (2021) in Saudi Arabia and Boyko et al., (2018) in the United States reported peripheral vascular

diseases and arterial disease as key LLA risk factors. Furthermore, Sadriwala et al., (2018) from India and Shahine et al., (2022) emphasized that diabetic neuropathy, coupled with vascular abnormalities, could increase LLA risk.

**Neuropathy:** Boyko et al., (2018) highlighted sensory neuropathy as an independent LLA risk factor. This is in agreement with systematic reviews by Rodrigues et al., (2022) and Bandarian et al., (2022) which identified peripheral neuropathy as a significant predisposing factor for LLAs among diabetic patients.

**Renal Disorders and Kidney Diseases:** Recent studies have cited renal disorders as the strongest LLA risk factors. Hallström et al., (2021) from Sweden associated renal dysfunction with amputation, while Rodrigues et al., (2022) included renal impairment as a factor related to LLA. Similar findings have been reported in the Arabian region with Shatnawi et al., (2018) in Jordan and Alkenani et al., (2021) in Saudi Arabia linking chronic renal impairment with increased major LLAs.

**Osteomyelitis:** Research indicates that osteomyelitis and chronic foot ulcers can potentially lead to amputation. According to Shahine et al., (2022) in Saudi Arabia and Lin et al., (2020), osteomyelitis is a significant LLA risk among diabetic patients. Further evidence is provided by Walicka et al., (2021) and Ha Van et al., (2020) in France, where a history of osteomyelitis was considered a strong amputation risk factor. This has been reinforced by studies in Korea by Lee et al., (2020) and Nigeria by Ugwu et al., (2019), who found a clear association between osteomyelitis and LLA risk among diabetic patients.

**Diabetic foot and Ulceration as risk factors of LLA:** The most recent research suggests that the incidence of diabetic foot ulcers (DFUs) is highest among males, those with a longer history of diabetes, and patients who have previously experienced ulceration or amputation (Al-Mohaithef et al., 2022; Dhanraj et al., 2021; Miranda et al., 2022). In a study by Al-Mohaithef et al. (2022) conducted in Egypt, which included 200 diabetic adults, it was concluded that patients with a history of ulceration or amputation were more susceptible to DFUs.

Other risk factors for DFUs included old age, male gender, diabetes duration of more than 10 years, being widowed, employed, illiterate, rural residency, obesity, uncontrolled blood sugar, insulin therapy, and smoking. This aligns with the findings from India by Dhanraj et al. (2021), which also noticed a higher incidence of foot lesions in older diabetic patients, particularly those between 61-70 years of age.

Further supporting these observations, Fawzy et al. (2019) identified older age, extended illness duration, and poor glycemic control as significant factors associated with Diabetic Foot (DF) in Saudi Arabia. Additionally, Miranda et al. (2022) noted that male patients with a longer duration of illness and lower socio-economic status are most prone to ulcers.

Concerning the risk of LLA due to DFUs, AlMehman et al. (2022) stated that diabetic complications and diabetic foot were the main reasons for LLAs among patients in Saudi Arabia. This has been echoed by Musa et al. (2018), who found that ischemic ulcers were less likely than neuropathic ulcers to result in amputations among diabetics.

Several studies from around the world, such as those by Kumar et al. (2018) in India, Ugwu et al. (2019) in Nigeria, and Lee et al. (2020) in Korea, have linked diabetic foot complications, prolonged ulcer duration, certain ulcer locations, and percutaneous transluminal angioplasty lesions to a higher risk of amputation.

Walicka et al. (2021) in Poland and Lin et al. (2020) provided similar insights, emphasizing that the main cause of LLA in diabetics is vascular pathology, primarily atherosclerosis, with soft tissue infections and ulcerations also being common triggers. A history of foot ulcers or gangrene is also considered a substantial risk factor for amputation in diabetic patients.

Research from China by Guo et al. (2019), as well as from India and Jordan by Sadriwala et al. (2018) and Shatnawi et al. (2018) respectively, has highlighted that higher Wagner's grades are a significant risk factor for LLA among diabetic patients. Confirming this, Dhanraj et al. (2021) stated that the likelihood of local or major amputation is estimated to be around 60% for patients with Wagner’s grade 2 through 5.

### Implications for Nursing Practice

The comprehensive understanding of risk factors associated with LLA among diabetic patients, as derived from our extensive literature review, carries profound implications for nursing practice.

Age, Gender, and Socio-demographic factors: With older age and male gender identified as significant risk factors for LLA, specialized attention must be provided to this demographic within the diabetic patient population. Additionally, socio-demographic factors such as marital status and education level should be factored into a patient's care plan. Educating families on the importance of assisting with foot care and addressing psychosocial aspects of the illness can also be highly beneficial.

Health Behaviors: As body weight, smoking, and alcohol consumption emerged as risk factors, lifestyle modification education and support should be incorporated into nursing practice. This includes offering patient education on the importance of maintaining a healthy weight, smoking cessation, and responsible alcohol use.

Management of Comorbidities: Diabetic patients with comorbidities such as cardiovascular diseases, neuropathy, renal disorders, and osteomyelitis require particular attention. Nurses should monitor these patients closely and provide education on managing

these conditions to reduce the risk of LLA.

Diabetic Foot Care: Considering the strong correlation between diabetic foot ulcers and LLA, nurses should be proficient in the assessment, treatment, and care of diabetic foot ulcers. They should also educate patients on proper foot care to prevent ulcer development and progression.

Patient education and counselling: Nurses have a key role in educating diabetic patients about their disease and its potential complications. Regular patient counselling about the importance of strict glycemic control, regular foot examination, importance of early detection of foot abnormalities, the impact of unhealthy habits such as smoking, the risks of obesity and the benefits of regular exercise and healthy diet are crucial for preventive care.

Interprofessional Collaboration: Finally, the management of diabetes and the prevention of LLA require an interprofessional approach. Nurses should work collaboratively with physicians, dietitians, social workers, and other healthcare professionals to provide comprehensive care to diabetic patients.

**Literature Review Gap**

Despite the extensive research on risk factors for LLA among diabetic patients, there is a lack of comprehensive studies specifically focusing on the Saudi Arabian population. While several international studies have identified demographic, clinical, and lifestyle-related factors associated with LLA, the unique sociocultural context and healthcare system in Saudi Arabia may contribute to different risk profiles. Additionally, there is a need for studies that examine the combined effect of multiple risk factors and their interactions, as well as the potential mediators and moderators of these relationships. Understanding the specific risk factors for LLA in the Saudi Arabian population can aid in the development of targeted interventions and preventive strategies to reduce the burden of diabetes-related amputations in this high-risk population. Moreover, further investigation is required to explore the impact of cultural factors, access to healthcare, and healthcare disparities on the risk of LLA among diabetic patients in Saudi Arabia. By addressing these gaps, researchers and healthcare professionals can contribute to the development of more effective interventions and policies to prevent LLAs in this population.

**Limitation**

Scope of the Literature Reviewed: Our study was limited to literature that was accessible in English and published within a certain timeframe. As a result, important research in other languages or published outside our chosen time frame may have been overlooked.

Publication Bias: This study is subject to potential publication bias, as research that finds significant results tends to be published more often than research that does not. Thus, our results may be skewed towards showing more substantial effects.

Heterogeneity in Study Design: The included studies vary significantly in their design, populations studied, and the definitions of risk factors and outcomes used. This heterogeneity could potentially impact the results and make it more difficult to draw definitive conclusions.

Lack of Individual Patient Data: Since we did not have access to individual patient data, we could not perform a more detailed analysis of the risk factors for LLA in the diabetic population.

Residual Confounding: Despite our attempts to control for confounding variables, there is a potential for residual confounding due to unmeasured or inaccurately measured variables.

Generalizability: The studies included in this review were conducted in a variety of settings and countries, which may limit the generalizability of our findings to other populations.

## CONCLUSIONS

Through an extensive review of relevant literature, this study has brought to light the multifactorial nature of the risks associated with LLAs among patients with diabetes. Identified risk factors range from demographic variables such as older age and being male to disease-specific factors like duration of diabetes and poor blood glucose control. Lifestyle choices such as smoking and obesity also contribute to this risk, along with various associated comorbidities.

The role of diabetic complications in LLA risk cannot be ignored, with peripheral neuropathy, cardiovascular and renal disorders, the presence of foot ulcers, and osteomyelitis significantly influencing the likelihood of amputation. Patients with a history of foot ulcers or previous amputations are particularly at risk. Given these findings, the importance of adopting a comprehensive, patient-centred approach in diabetes care becomes paramount. Healthcare professionals, including nurses, must prioritize routine foot care education, early detection and management of foot ulcers, maintaining optimal blood glucose levels, effective comorbidity management, and the promotion of healthy lifestyle habits.

Future research endeavours should aim to validate these risk factors across varied patient populations and formulate effective, risk-based interventions. As we continue to enhance our understanding of these risks, healthcare professionals will be better equipped to devise preventative strategies, ultimately improving the quality of life for diabetic patients and reducing the incidence of LLAs.

**Supplementary materials**

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**Conflict of interest**
The authors of this paper state that they have no financial or non-financial conflicts of interest related to the publication of this research.



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