Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 905–912

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Review

A review on diabetic foot challenges in Guyanese perspective

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ARTICLE INFO

Article history:
Received 26 November 2018
Accepted 19 December 2018

Keywords:
Diabetes
Diabetic foot
Guyana

ABSTRACT

Background: Diabetes mellitus signifies a major public health threat worldwide. Type 2 diabetes has been reported as the fourth leading cause of death and has affected 15.5% of the adult population in Guyana, South America. Diabetes has also led to major lower extremity amputation at the only referral public hospital in Guyana. Diabetic foot and related complications are known to be multifactorial. Conclusion: In this review, we highlight the information on the diabetic foot and related complications with an emphasis on Guyanese background.

1. Background

Diabetes mellitus is a group of metabolic diseases which represents a major public health threat worldwide. Diabetes mellitus (DM) is also a chronic disease characterized by high plasma glucose concentrations due to inability of the body to adequately produce or use insulin effectively [1]. Most times the disease is diagnosed when there is high plasma glucose concentration or impaired glucose tolerance [1]. Diabetes is known to cause many complications but one of the serious complication of diabetes is the development of foot ulcer. DM is categorized into three types. Type 1 diabetes (T1DM) is caused by an autoimmune reaction, during which the body's defense system attacks the insulin-producing beta cells in the pancreas also called as insulin dependent diabetes mellitus (IDDM). IDDM mostly starts in persons above 40 years of age [1]. Type 2 diabetes (T2DM) is known to be the most common type of diabetes. T2DM also known as non-insulin dependent diabetes mellitus is referred to as late onset diabetes. In T2DM, the body still produces insulin but becomes resistant so that the insulin is ineffective to the body. Over time, insulin levels may subsequently become insufficient. Most common form of DM is T2DM, which constitutes about 90%–95% of all diabetes in developed countries and accounts for an even higher percentage in developing countries [1]. The economic consequences, for both patient and society, are very large and every effort to improve care of these patients is worthwhile. The third type is gestational diabetes mellitus (GDM) is characterized by intolerance to glucose which is seen during pregnancy after performing an oral glucose tolerance test [2]. Most of the time GDM returns to normal after delivery. But in certain scenario were pregnant women has a family history of diabetes, increasing maternal age, obesity and coming from ethnic group with high risk of developing T2DM, can develop permanent diabetes. The babies of such mothers also falls under high risk of becoming obese and could most times have impaired tolerance to glucose [2,3]. American Diabetes Association (ADA) define DM as hyperglycemia due to defects in insulin secretion, insulin action, or both [4]. In this article, we review available evidence on complications of DFU with an emphasis on Guyanese perspective.

2. Methods

For the purpose of this review, all studies selected have been conducted in an outpatient setting, been published in English language, have a primary focus on Caribbean and Guyana and have been published. The key terms used to extract articles were *diabetes, adult, Caribbean, diabetic foot, education.*

3. Diabetes status and its consequences

3.1. Global status

World Health Organization (WHO) estimates a prevalence of 422 million people with diabetes worldwide of which 1.6 million deaths directly attributed to diabetes each year [5]. This estimate is projected to rise to 642 million by the year 2040 [1] and most of the

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https://doi.org/10.1016/j.dsx.2018.12.010
1871-4021/

people with diabetes (79%) are living in low and middle income countries. It is also shocking that greatest number of people with diabetes fall between 40 and 59 years of age [6]. In 2012, diabetes was the direct cause of 1.5 million deaths [6]. Additional 2.2 million deaths were due to higher-than-optimal blood glucose causing risks of cardiovascular and other diseases. In low and middle income countries, diabetes related death occurs prior to age 70 compared to high-income countries [6]. Recent study by IDF (International Diabetes Federation) claims that diabetes caused 4 million deaths. Surprisingly, more than 80% of diabetes and related deaths occur in low and middle income countries. WHO projects that diabetes will be the 7th leading cause of death by 2030 [8]. Diabetes is also known to cause premature death and disability. UN had reported it as one of four priority non communicable diseases (NCDs) targeted by world leaders in the 2011, Political declaration on the Prevention and Control of NCDs [9]. Some studies have further claimed that developing countries will contribute to more than 75% of the overall increase with majority falling between 40 and 59 years of age [1,10,11]. Change in life styles and urbanization are two major reasons to be blamed for increase in the number of DM cases [12,13].

3.2. Caribbean status

Caribbean is defined as consisting of 28 countries and territories [14]. Three mainland countries Belize, Guyana and Suriname due to similar cultural and historical reasons, considered part of the Caribbean. They are also members of Caribbean Community (CARICOM). Similar to global scenario, DM is one of the major public health challenges for the Caribbean in the twenty-first century [15]. DM is estimated to affect between 10% −15% of the adult population in the Caribbean region [16], and considered to be a major contributor to premature mortality [16,17]. With rapid transition and increasing westernization in the Caribbean, type 2 diabetes has become a major public health burden and its prevalence and incidence in the region is higher than many developed countries [18]. IDF estimates 54 million adults with IGT (impaired glucose tolerance) in North America and Caribbean region with 35% being undiagnosed [6].

3.3. Guyanese status

Guyana is an English-speaking country which was a former British colony located on the northern coast of South America. The majority of the population of Guyana lives in the capital city of Georgetown and along a narrow coastal strip. Other parts of Guyana has a sparse population. Guyana is ethnically diverse, most of its populations are of South Asian, African and/or Amerindian heritage. Guyana is culturally and economically tied to the Caribbean nations and is classified as a Caribbean country by the IDF [19]. Guyana was classified as a lower-middle-income economy until 2016 but now classified as an upper middle income country and is in a state of epidemiological transition [20–22]. Guyana is also the third poorest country in South America therefore suffer frequent migration of expertise and thus face scarcity of health care expertise [23,24]. Although diabetes is highly prevalent in Caribbean countries, Guyana has a second highest prevalence (15.9%) of diabetes in Americas [19,25–30]. Diabetes was recorded to be the fourth leading cause of death in Guyana during 2008 with an increase of prevalence to 15.5% during 2011 [31,32]. Guyana's health system has a comprehensive medical care system of regional and district hospitals, community health centers, and rural health posts. Georgetown Public Hospital cooperation (GPHC) is a public teaching hospital that is the major tertiary care center for the country. GPHC offers free medical care which includes essential medications for diabetes and also available at all Ministry of Health (MOH) centers. A study done in Guyana found high burden of low health literacy and diabetes in Guyana and other low- and middle-income countries, could relate to blood glucose among patients without diagnosed diabetes [33]. Diabetes and diabetic foot disease has become so common in Guyana that the primary Guyanese referral hospital has a clinic specializing only in diabetic foot ulcer evaluation and treatment, and satellite diabetic foot clinics have been established in some regional hospitals and health centers [33].

3.4. Definition of diabetic foot

The definition of the diabetic foot has been described as infection, ulceration and/or destruction of deep tissues associated with neurological abnormalities and various degrees of peripheral vascular disease [34,35]. As indicated by this description, it may involve one or more of these conditions, and they follow conditions. A diabetic foot ulcer is the general term to describe a full-thickness wound below the ankle in a patient with diabetes [34]. The major adverse outcomes of diabetic foot problems are foot ulcers and amputations, and foot problems account for more hospital admissions than any other long-term complications of diabetes, which also results in increasing morbidity and mortality [36,37]. Diabetic foot ulcers are therefore a major concern of diabetic patients as it prevents person from quality of life both socially and economically [38]. Foot problems are indeed a global problem and do not discriminate based on country or economic status. All countries which reports diabetes also reports DFU and related consequences, mainly of neuropathy and peripheral vascular disease. The prevalence of foot ulcers ranges between 4% and 10% globally among persons diagnosed as having diabetes mellitus [39]. Diabetic patients are believed to have a 12–25% lifetime risk of developing a foot ulcer [40]. DFUs, once infected could lead to neuropathy, ischemia, poor wound healing and are the most common cause of diabetes-related hospital admissions [35]. Moreover, diabetic foot could cause tissue breakdown resulting in morbidity and possible amputation [40,41]. More of concern is due to the fact that it takes a toll on patient's quality of life in terms of social and economic stand point [38].

3.5. Epidemiology of DFU

3.5.1. Prevalence and incidence

The prevalence of diabetic foot ulcers is described to be between 4% and 10% of the diabetic population, with a lifetime risk of up to 25% [39]. This statistic has changed in 2016, WHO reports that the rates of amputation in populations diagnosed with diabetes are typically 10 to 20 times than those of non-diabetic populations which shows a change over the past decade. Some ethnic groups such as South Asian and African lineage, diabetes tends to cluster due to genetic predisposition and social deprivation [42,43]. This complex combinations of genetic and environmental factors as well as social deprivation make DM to take a lead of about six times more common among people of South Asia descent and about three times more common in people of African and African–Caribbean lineage [42,92,93]. Some other studies have also associated risk of developing a foot ulcer with ethnicity [44–46]. For example some studies carried out in the UK suggest that people of Asian subcontinent origin are less likely to develop foot ulcers and/or undergo amputation than Caucasians [47,48].

The incidence of foot ulcers in diabetic patients varies between 2 and 6% in Western Europe and North America, and between 19% and 29% in the Middle East [49]. A similar study done in EURODIALE showed that there are noticeable regional differences throughout Europe about diabetic foot ulcer and amputation occurrence

[50,51]. Foot infections are known to stand as number one cause of hospital admissions to the surgical wards in Caribbean public hospitals and of amputations which frequently result in mortality [52–55]. A DFU study from Barbados reported that five year survival of a diabetic patient after a lower limb amputation was only 44% compared to 82% among those without amputation [56]. It is well documented that until 2008, diabetic foot complications were the most common admitting diagnosis at Guyana's public hospital with 42% of cases having a lower extremity amputation (LEA) [57–59]. It's not surprising that diabetic foot complications are very common in countries of the Caribbean. Studies from Barbados reports a LEA of 936/100,000 diabetic population were as Trinidad reported 12% with previous foot ulceration and 4% amputation [60,61]. Similarly a study in Jamaica reported a higher prevalence of 8.5% for amputation [62].

3.5.2. Diabetic foot classification

There are several classification systems for DFUs, three being the most commonly used [44,63,64], each with their benefits and limitations. Lipsky et al defined DFU as any inframalleolar infection in an individual with diabetes mellitus. To define inframalleolar infections, they are cellulitis, myositis, abscesses, necrotizing fasciitis, septic arthritis, tendonitis, osteomyelitis and paronychia [65].

The Wagner classification system for foot ulcers is widely used, and was most commonly used one [63].

The Texas Diabetic Wound Classification System [44) includes wound depth, the presence of infection and PVD in every category of the wound assessment.

The PEDIS classification system [64] includes the categories: Perfusion, Extent/size, and Depth/tissue loss, Infection and Sensation, with a grading system for each category.

3.5.3. Diabetes and expenditure

Diabetic foot and related consequences are known to have a global economic cost of billions of dollars with respect to treatment, lengthy hospital stay and subsequent amputation [66,67]. Such complex combinations of predisposing factors are largely responsible for ulceration and amputation. According to IDF, the mean healthcare expenditure due to diabetes per person with diabetes is 82.4 USD. It has been estimated that 80% of the total expenditure on diabetes treatment and prevention is spent only in developed countries while the middle and low income countries accounts for less than 20% of total expenditure even though the latter countries account for 70% of morbidity and mortality of the disease Fig. 1 [1]. There has variation in expenditure among different age groups and gender. In 2010, three-quarters of the world's expenditure were used for persons among 50 and 80 years. Moreover, more money was expected to be spent on diabetes care for women than for men [68]. A study done to evaluate status of amputations among diabetic patients found that both the physical dimension scores and the total sickness impact profile (SIP) scores were significantly higher for amputees. This study therefore demonstrates the detrimental physical and psychosocial health status of patients with diabetic-related LEA [69].

The cost of DM was estimated at US$ 65 billion in 2000 in Latin America and the Caribbean (LAC) [70]. A recent study to estimate the economic cost of diabetes in countries of LAC was done by Barcelo et al in 2015 [71]. The study claimed over 41 million adults (20 years of age and more) with DM in LAC. It further subcategorize as total indirect cost to be US$ 57.1 billion, of which US$ 27.5 billion was due to premature mortality, US$16.2 billion to permanent disability, and US$ 13.3 billion to temporary disability. On average, the annual cost of treating one case of DM in LAC was estimated between US$ 1088 and US$ 1818 [71]. Guyana reportedly spend USD $361 per case, the lowest among LAC. Recently IDF has released a report which claims half the global diabetes healthcare spending occurs in the NAC. Guyana only estimates an expenditure of 356.4 USD/patient [6].

Wagner Classification	
Grade	Description
Wagner grade 0	No ulcer
Wagner grade 1	Superficial ulcer (up to but not through dermis)
Wagner grade 2	Ulcer extension involving ligament, tendon, joint capsule or fascia (no abscess or osteomyelitis)
Wagner grade 3	Deep ulcer with abscess and/or osteomyelitis
Wagner grade 4	Gangrene of portion of the foot
Wagner grade 5	Extensive gangrene of the foot

University of Texas Classification	
Stages	Description
Stage A	No infection or ischemia
Stage B	Infection present
Stage C	Ischemia present
Stage D	Infection and ischemia present
Grading	Description
Grade 0	Epithelialized wound
Grade 1	Superficial wound
Grade 2	Wound penetrates to tendon or capsule
Grade 3	Wound penetrates to bone and joint

3.5.4. Risk factors of diabetes

People living with diabetes are known to encounter a number of health issues like cardiovascular diseases (CVD), blindness, kidney failure, and lower limb amputation. It has been well documented that CVD is the most common cause of death among people with diabetes. People with diabetes carry a risk of amputation which could be more than 25 times greater than that of people without diabetes [6]. Diabetic foot ulcer patients have a greater than twofold increase in mortality compared with non-ulcerated diabetic patients and it was well reported that ischemic heart disease is the major cause of premature mortality [72].

Peripheral neuropathy and Peripheral vascular disease (PVD) are the two factors most commonly attributed to DFU. DFU are therefore often described as of neuropathic, ischaemic, or neuroischaemic origin [34]. The cause of diabetic foot ulcers are often multifactorial. Sensory loss, foot deformities, repetitive pressures and skin breakdown are considered to be the key aetiopathogenetic pathways to neuropathic foot ulcers in diabetes. Addressing these issues would be a cornerstone in the management of plantar diabetic foot ulcers [73,74]. Visual impairment, reduced joint mobility, callosities, present or previous foot ulceration, and previous amputation have also been described as factors contributing to the development of DFU [34,47,75]. Up to 70% mortality after 5–10 years has been reported [7,77,78]. Outcome of diabetes related mortality have been made complicated due to the fact that around half of the patients will have died by 5 years and above [77–80]. The high mortality rate among these patients justifies consideration and further highlights the general morbidity of this patient group. Studies have also highlighted that patients with depressive symptoms and a new DFU had a higher mortality than patients who did not exhibit signs of depression [81]. Apart from increased mortality, the most serious immediate adverse outcome is a lower limb amputation. It has been claimed that every 30 s a lower limb is amputated due to diabetes [34]. Up to 70% of all LEA are done in people with diabetes and 85% of these amputations are preceded by

PEDIS classification system						
Grade	Perfusion	Extent	Depth	Infection	Sensation	Score
1	No PAD	Skin intact	Skin intact	None	No loss	0
2	PAD, No CLI	<1 cm^2	Superficial	Surface	Loss	1
3	CLI	1–3 cm^2	Fascia, muscle tendon	Abscess, fasciitis, septic arthritis		2
4		>3 cm	Bone or joint	SIRS		3

PAD, peripheral arterial disease; CLI, critical limb ischemia.

a foot ulcer [34,82].

Looking at the alarming LEA of 42% diabetic patient at GPHC a Guyana Diabetes and Foot Care Project (GDFP) was developed and was funded by Canadian International Development Agency (CIDA). A simplified 60-s screening tool was also developed that identified patients who have high risk of developing foot ulcers. And after identifying such patients, they were later referred for more intensive surveillance [39,58]. It has been reported that men in Guyana are reluctant to come for diabetes screening although a higher percentages are admitted for foot complications. Moreover patients presented late for treatment because of poor knowledge [83]. Other risk factor is its higher prevalence among women than in men. In Ghana, women's were about 2.5 times more prevalent than in men [84–86]. Similar findings were reported from other parts of the world, in Mauritius, India and China [87–89]. Contrary to this, prevalence of DM among men were slightly higher than women in developed countries like the UK and the USA [43,90,91]. Similar to DM, DFU was more prevalent in diabetic women than in men contrasting in developed countries where it is more common in men than in women [48].

A systemic review done in Caribbean, on the distribution of gender among diabetes found a higher prevalence of DM in women than in men although in two studies this was not statistically significant ($p > 0.05$). Most studies reported men had lower mean BMI values than women. In addition to higher BMI, women in the Caribbean region had risk of obesity, and consistently lower levels of physical activity. Therefore it is important to implement policies aiming such risk factors in the region to prevent diabetes and associated risks [94].

3.5.5. Diabetic foot infection

According to Lipsky et al, the infected diabetic foot malperforans ulceration is a prominent and typical lesion. The presence of an ulcer in diabetic foot increases the susceptibility of the wound to infection from bacteria. Due to contiguous extension an active infection progresses from bacterial colonization to involving deeper tissues to limb–threatening infection beyond 2 cm [65,66]. Due to weak immunity, poor blood circulation or impaired tissue perfusion, risk and severity of foot infections increases among diabetic foot patients [95]. Although infection is rarely the direct cause of a diabetic foot ulcer, in the EURODIALE study, 25–75% of patients at various centers were considered to have a wound infection on the time of admission [36]. Infection in the diabetic foot intensifies the risk of hospitalization and of a consequent amputation, especially in combination with PVD [36,96–98]. One of the culprit in DF is DFI (diabetic foot infection) following the traumatic injury with introduction of bacteria. The diabetic foot infections are poly-microbial, harboring anaerobic organisms together with aerobes [99]. Failure to distinguish and control of the infectious process could lead to devastating consequences like limb amputation, sepsis, and mortality [100]. Infection of diabetic wounds are often by multidrug resistant organisms (MDRO] which makes them obstinate to healing. There are many studies done on epidemiology of diabetic chronic wound infections. Predominant aerobes reported in most studies are *Staphylococcus aureus*, coagulase-negative staphylococci, Streptococcus species, Enterococcus species, Corynebacterium species, Enterobacteriaceae, and *Pseudomonas aeruginosa* [101]. In chronic wounds, microbial bio burden are reported due to 3 factors namely; microbial load, microbial diversity and presence of potential pathogens [102]. Bacterial ecology of DFIs are found to be affected by the interaction of environmental, person's hygiene and cultural concerns relating to a geographical region [102]. It is therefore very important in terms of treatment for the healthcare providers to be familiar with the microbial population in their geographical settings [101,103].

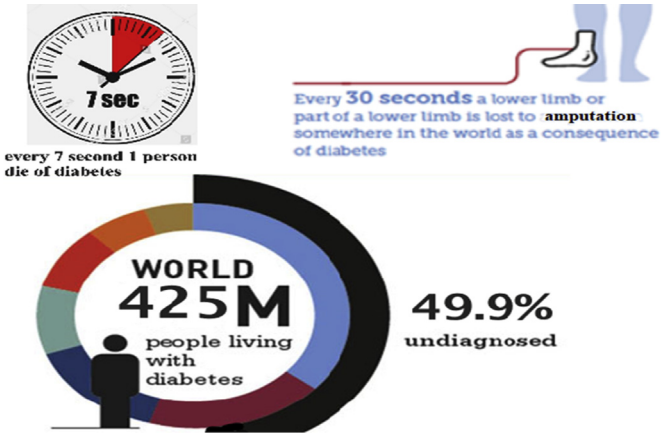

Fig. 1. Risks and status of diabetes (adapted and modified from IDF 2018).

3.5.6. Prevention and care

One of the important precautions to help reduce the complications of diabetic foot are patient education, blood sugar control, wound debridement, advanced dressing, offloading, advance therapies [104]. Prevention of diabetic foot ulcers also includes regular inspection and examination of feet at risk, education of patients and relatives, and off-loading with custom-made insoles and individually adjusted footwear [34,105]. The basis for management of the diabetic foot ulcer is the multidisciplinary team, which includes medical and surgical treatment, podiatry, nursing and orthotic support [34,106]. The multidisciplinary team treatment of diabetic patients with foot ulcer has been shown to be cost-effective, improves healing rate, and reduces amputation rate and ulcer recurrence [107–112]. There is no doubt that the quality of life of people living with diabetes can be greatly improved with the implementation of self-management education [76,113]. Treatment of metabolic disturbances, malnutrition, peripheral vascular disease, infection, pain, and oedema as well as topical treatment with ulcer dressings, off-loading, vascular assessment and surgery, and orthopedic surgery (major debridement, minor and major amputation) are all important parts of the multidisciplinary team approach [106]. The International Working Group on the Diabetic Foot and other professional bodies recommends that appropriate

foot care and footwear possibly will reduce the risk of foot ulceration and amputations [114,115].

3.5.7. Treatment

Clinical practice guidelines and Infectious Disease Society of America suggests that the choice of antibiotic should and always be guided by the history, clinical examination, severity of infection, causative agent and history of previous antimicrobial sensitivity pattern for the diagnosis and treatment of diabetic foot infection [116]. Bacterial resistance from diabetic foot to first line antibiotics such as ampicillin, gentamicin and ciprofloxacin has been widely reported [117]. The fact that, lack of dedication and specialized diabetic foot care units could lead to wrong DFI treatment. This would include treatment of DFI without culture and anti-microbial sensitivities done or antibiotics prescribed for wrong duration. Although lower limb amputation is considered to be possibly preventable [118], lack of knowledge and inappropriate foot care practices like barefoot walking, inappropriate footwear, poor foot hygiene and delay in seeking medical attention lead to the complications of diabetic foot [119]. It is of no wonder that several studies have shown that a majority of people with diabetes do not receive guideline-recommended foot care, including regular foot examinations [120]. Even in the developed country like United Kingdom, 33% of people with diabetes do not recall receiving information about foot care [118]. It is important to note that patient of high risk group should receive enhanced and focused foot care education [99].

3.5.8. Awareness

Most countries reports spending millions of dollars for diabetes and related complications, still the prevalence of diabetes and its complications are raising high every year. One major reason would be that even though persons are educated on diabetes and to prevent complications at clinical visits, the interest tend to vane over time and patients won't feel the same encouragement. The study done in Barbados reports, barriers, like limited resources, priority to other diabetic complications, and reliance on self-care ability, eclipse the complications of diabetic foot. It also identified the fact that patient's instinct towards diabetes and foot care decrease over time [120]. Although the International Working Group on the diabetic foot acknowledges the limited evidence on long term efficacy of patient education, it also recommends some form of patient education to improve their foot care knowledge and behavior [121]. Studies have reported that training and self-management is an essential part of the treatment of diabetes [122]. Patient education is the most constructive track that could assist with early detection, lessen the complications, and assist with the management of diabetes [123]. However, inadequate knowledge regarding complications of diabetes tend to decrease awareness and may lead to high economic burden in terms of management of complications. The fact that low health literacy among patients with diagnosed diabetes may be associated with elevated blood glucose due to poor diet and lifestyles choices or health behaviors, difficulty performing disease self-management tasks, or poor medication adherence [24,124–126]. A research done on patients with unknown diabetes in Guyanese emergency department found that lower patient-reported health literacy was associated with elevated HbA1c, and the c-statistic for random blood glucose and HbA1c $\geq$ 48 mmol/mol as 0.94 [33]. Moreover, patients may feel education is not worth the cost (i.e., patients have to incur the cost of transportation to/from the clinic on a separate day). Those with foot problems, especially painful peripheral neuropathy, may not be able to visit the clinic frequently. These patients may opt to make just one trip, often the one in which they will be getting prescriptions for their medications. For these reasons, Ward et al. recommended a flexible schedule for diabetes education, offering education at any time for the maximum convenience of patients rather than focusing on health care provider's convenience, preferably integrating it into normal consultation [127]. Educational programs should also address psychological and cultural factors that often underlie self-care behavior [128].

4. Conclusions

Diabetic foot infections are a major public health problem and early diagnosis and appropriate treatment are essential. In this review, we have highlighted the difficulties of diabetic foot and related complications especially in low income country like Guyana which has multiethnic population. Further research could reveal the patient's education in terms of emphasize on foot care education, again implementing the policies that are available to control the disease and minimize further complications.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Authors' contributions

RK prepared the outline of manuscript. All authors read and participated in the final manuscript.

Acknowledgements

Not applicable.

Abbreviations

DM	Diabetes mellitus
T1DM	Type 1 diabetes
IDDM	Insulin Dependent Diabetes Mellitus
T2DM	Type 2 diabetes
GDM	Gestational Diabetes Mellitus
ADA	American Diabetes Association
WHO	World Health Organization
IGT	Impaired Glucose Tolerance
IDF	International Diabetes Federation
GDFP	Guyana Diabetes and Foot Care Project
CIDA	Canadian International Development Agency
GPHC	Georgetown Public Hospital cooperation
MOH	Ministry of Health
PVD	Peripheral vascular disease

LEA	Lower Extremity Amputation
SIP	Sickness Impact Profile
LAC	Latin America and the Caribbean
CVD	Cardiovascular Diseases
MDRO	Multidrug Resistant Organisms

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.12.010.

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