British Journal of Medicine & Medical Research
20(3): 1-14, 2017; Article no.BJMMR.31547
ISSN: 2231-0614, NLM ID: 101570965

SCIENCEDOMAIN ***international***
www.sciencedomain.org

Diabetes Complications and Burden in a Metropolitan Environment: Correlates and Costs of Diabetic Foot Disorders

Raouf M. Afifi[1,2,3*], Ashraf El-Ghali Saad[4], Yousef Afifi[1] and Same Zaytoun[5,6]

[1]Community Health Research Institute, International Management-Health Service, Indianapolis, Indiana, USA.
[2]Saudi Board of Community Medicine Center, Armed Forces Hospitals, Taif, KSA.
[3]Community Health Research Excellence Center, Cairo, Egypt.
[4]Preventive Medicine Department, Armed Forces Hospital at Wadi Al-Dawasir, KSA.
[5]Department of Community Medicine, School of Medicine, South Valley University, Qena, Egypt.
[6]Department of Public Health, Batterjee Medical Academy, Jedda, KSA.

Authors' contributions

This work was carried out in collaboration between all authors. Author RMA conducted study design, performed statistical analyses, conducted literature review, wrote the methodology, results display and discussion, and wrote the first draft of the manuscript. Author AES shared in study design, data collection procedure, discussion and recommendations, and preliminary statistical analyses. Author YA conducted data entry and backup, and shared in writing introduction, final report writing, editing, and referencing. Author SZ managed data collection sourcing plan, ethical approvals, and referencing. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2017/31547
Editor(s):
(1) Domenico Lapenna, Department of Medicine and Aging Sciences, University "G. d'Annunzio" Chieti-Pescara, Chieti, Italy.
Reviewers:
(1) Maria Demetriou, Democritus University of Thrace, Greece.
(2) Sonali Kar, KIIT University, India.
(3) Chandrashekhar Mahakalkar, Jawaharlal Nehru Medical College, India.
(4) Estrella Cervantes García, National Autonomous University, Mexico.
Complete Peer review History: http://www.sciencedomain.org/review-history/18124

Original Research Article

Received 12th January 2017
Accepted 1st March 2017
Published 9th March 2017

ABSTRACT

Background: Diabetes is a chronic disease of complications, and of which diabetic foot ulceration (DFU) and consequences can be devastating.
Aim: Identify and analyze the economic costs related to DFU upon the Saudi diabetic population.

**Corresponding author: E-mail: raoufafifi43@gmail.com;*

Methods: Direct costs related to treatment of DFU illness episodes in patients enrolled in healthcare plans with major health insurance agencies in Saudi Arabia between 2012 and 2015 were studied. Patient demographic characteristics, treatment and intervention level, and cost of illness (COI) were analyzed.

Results: The enrollees' age averaged 54.33 ±4.76y (range 41-to-72=31y). Out of 229 diabetic patients surveyed, 158 (68.9%) were male; 162 (71%) were Saudis and 67 (29%) were non-Saudis. Least frequently needed intervention for DFU conditions was conservative treatment alone (12%, n=28), mostly needed was debridement (43.2%, n=99), and in-between was either minor lower extremity amputation (LEA) (26.2%, n=60) - or major LEA (18.3%, n=42). Further, amputation increased by age, 1.7% minor LEA for DFU patients <50 years old and 0.9% LEA for ≥50y old peers *(Fisher's exact=27.5, p<0.0001).* Also, amputation was more frequent among Saudi DFU patients compared to non-Saudi peers (23.6% vs. 2.6% minor LEA, and 14.4% vs. 3.9% major LEA, respectively) *[Fisher's exact 17.3, p=0.0015].* The enrollees' mean COI accounted SR35,934.4±15,065.1 (range 141,204, 11,032 -to- 15,2236) (1SR=USD267) per DFU event, which significantly varied by the level of intervention *[F(df 3, 225)=426.9, p<0.001].* Saudi DFU patients significantly incurred higher COI *[t(df 214.8)= 9.7, p<0.001].*

Conclusions: Among DFU patients, amputation rates and related COI increased both by patients' age and having Saudi nationality. An ongoing update on the prevalence and costs of DFU disorders should be among the community health research priorities in Saudi Arabia. Prevention and close monitoring save limbs and assure better quality of life of Saudi diabetic patients.

Keywords: Correlates; costs; diabetic; foot; Saudi Arabia.

1. INTRODUCTION

Diabetes mellitus (DM) is a serious disease that occurs either when the pancreas does not produce enough insulin (type 1 diabetes), or when the body cannot effectively utilize the insulin it produces (type 2 DM) [1]. The disease represents a major concern for healthcare systems, given the increase in incidence rates among almost all population subsets, disregarding the variability in the demographic or socio-economic status. In 2015, an estimated 415 million people had diabetes worldwide, with type 2 diabetes making about 90% of the cases [2]. This represents 8.3% of the adult population [3], and with nearly equal rates in both women and men [4]. Importantly, the current epidemiological profile of DM probably reflects a universally escalating tendency for risk factors, such as overweight or obesity. Mortality-wise, too, diabetes occupies the 8th position among causes of death due to non-communicable disease (NCDs) [5], accounting up to 1.5 million deaths in 2012. Higher-than-optimal blood glucose caused an additional 2.2 million deaths by increasing the risks of cardiovascular and other diseases. Out of these 3.7 million deaths, 43% occur before the age of 70 [5]. The toll of elevated blood glucose in those under 70 is now higher in low- and middle-income countries than in high-income countries (150 million vs. 0.3 million) [6]. Factoring the relatively limited healthcare resources and support these countries might be suffering, an unfavorable health and economic outcome is justified. The American Diabetes Association (ADA) defines diabetes as a *"group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both"* [7]. Diabetes is also identified in surveys as those having fasting plasma glucose (FPG) value ≥7.0 mmol/L (126 mg/dl) or on medication for raised blood glucose, involves a myriad of etiologic, deterministic, physiological, clinical, and prognostic characteristics, many of which can be crippling. Further, the ADA recommends that testing to detect type 2 diabetes in asymptomatic people, and "prediabetics", should be considered in adults of any age who are overweight or obese and who have one or more additional risk factors for diabetes. In which case, testing should begin at age 45 years [8]. If tests are normal, repeat testing carried out at a minimum of 3-year intervals is reasonable. Since DM is characterized by recurrent or persistent high blood sugar, PG ≥11.1 mmol/L (200 mg/dl) 2 hours after a 75-g load as in oral glucose tolerance test (OGTT) can also be used for diabetes diagnosis [8]. Further, symptoms of high blood sugar and casual PG ≥11.1 mmol/l (200 mg/dl) and hemoglobin A1C ≥48 mmol/mol (6.5%), all can also be basis for diagnosis [1]. A positive result, in the absence of unequivocal high blood sugar should be confirmed by a repeat of any of the above methods on a different day. The FPG is easy to measure and time saving compared to the OGTT which offers no prognostic advantage over FPG. As such, two FPG measurements above 126 mg/dl (7.0 mmol/l) is considered diagnostic for DM and people with FPG levels 6.1 - 6.9 mmol/l (110 to 125 mg/dl) are considered to have IFG, while people with PG ≥ 7.8 mmol/l (140 mg/dl) but not over 11.1 mmol/L in OGT testing are considered to have IGT [9,10,11].

1.1 Complications

The risk of type 2 diabetes is determined by interplay of genetic and metabolic factors. Ethnicity, family history of diabetes combined with age, obesity, unhealthy diet, physical inactivity, and smoking increase the disease risk [12,13]. Excess body fat, a summary measure of several aspects of diet and physical activity, is the strongest risk factor both in terms of clearest evidence base and largest relative risk. Complications of diabetes are increasingly stressing to medical, social, and economic planners. If not well controlled, diabetes can possibly lead to those complications affecting almost all body systems. By the time people are diagnosed, they frequently have developed complications, e.g., retinopathy or ischemic heart disease (IHD). Other body organs affected in diabetes include central nervous system (e.g., stroke), peripheral nerves (e.g., diabetic neuropathy), kidney (diabetic nephropathy), and DFU. Diabetes complications bring about substantial economic losses to patients and their families. These losses, as seen by the global economic cost of diabetes in 2014, total a staggering $612 billion [14]. While the major cost drivers are hospital and outpatient care, a contributing factor is the rise in cost for analogue insulins (derived from human insulin by modifying its structure to change the pharmacokinetic profile), which are increasingly prescribed, despite little evidence that they provide significant advantages over cheaper human insulins) [15].

1.2 Pathophysiology and Clinical Presentation of DFU

Diabetic foot problems develop due to a combination of reasons and mechanisms, important of which are pathologic changes of the nerve supply to the foot, augmented by ischemia as a result of peripheral vascular disease (PVD), due to “macroangiopathic” changes of the foot vasculature. Neuropathy and resulting parasthesia, coupled with mechanical factors are particularly dangerous as patients are at great risk of painless injury and subsequent FU [16]. Extrinsic ulceration is a result of trauma to the soft tissues from an extrinsic source such as tight fitting footwear or a lack of cushioning. In contrast, intrinsic ulceration is a result of abnormalities in the structure of the neuropathic foot which lead to deformities such as clawing of the lesser digits that increases the pressure on the metatarsal heads and dorsal inter-phalangeal joints [17]. This altered mechanics of the foot results in excessive pressures on the exposed plantar aspect of the foot which when walking causes formation of callous that in itself may cause high pressure [18], and ultimately leads to tissue damage and ulceration. Autonomic neuropathy can also lead to diabetic foot complications as it causes reduced sweating. This results in dry skin that is prone to cracks and fissures which then allows portal of entry for infection. Ultimately, the role of maintained hyperglycemia in the causation of PVD and peripheral neuropathy in diabetes and hence accelerates foot ulceration is evident [17,18].

1.3 Burden and Cost of Illness

Diabetic foot complications refer to a group of conditions which present with: foot ulceration, neuropathy, deformity, gangrene and/or ischemia and infection [19]. Particularly foot infections are the commonest cause of hospital admission in patients with diabetes and in many cases are the cause of lower extremity amputation (LEA). The annual incidence of DFU varies between 2.1 to 7.4% and with a lifetime risk of developing a DFU has been estimated at 25% [20]. If not timely and properly managed, the endpoint of DFU is amputation in 15% – 27%. When amputation happens, significant morbidity and mortality in addition to immense emotional, social, psychological and financial consequences ensues [21]. The intimate relationship between infection of the FUs and progression to gangrene and LEA makes diabetics at 10-20 times higher risk of experiencing amputation than the general population. Recently, a few high-income countries have documented a reduction in amputation rates in people with diabetes [22]. The derangement in the social, psychological, and health-related quality of life (HRQOL) inflecting diabetics with FU is truly painful. The expenditure against caring for diabetics with FU is five-times greater than that for non-ulcerative peers a year-time after the first DFU episode [23]. All health economies suffer from such costs, e.g., accounting 15% up to 40% of the world’s total healthcare expenditure (lowest in industrial countries and highest in developing ones) [24]. Individuals with DFU require more visits to healthcare facilities, and when admitted to hospital for inpatient care or surgery they tend to stay longer [20]. Particularly DFUs ending with LEA have been major drivers of diabetes-related direct health care costs [25,26]. For instance, the direct costs of inpatient care and prostheses for 42,424 DF disease (DFD) American patients undergoing amputation totaled $1.65 billion in annual direct costs of DFDs [26]. Ultimately, the high liability for complications renders people with diagnosed diabetes incur medical expenditures almost 2.3 times more than those without diabetes. In the US, too, indirect costs include absenteeism ($2.6 billion) and reduced productivity while at work ($20.0 billion) for the employed population, reduced productivity for those not in the labor force ($0.8 billion), unemployment from disease-related disability ($7.9 billion), and lost productive capacity due to early mortality ($26.9 billion) [27].

The term “cost of illness” is generally a measurement tool used for economic evaluation of a disease burden upon the patient, health system, and the society. The COI analysis includes some metrics of “health loss” and it also attempts to measure the costs incurred, e.g., in treating DFDs [28]. The issue is that in economic decision making, “cost” should be considered in contrast with benefit (as in cost-benefit analysis-CBA), with effectiveness (as in cost-effectiveness analysis-CEA), and with quality-adjusted life years (QALYs) or latent utility assessment (as in cost-utility analysis [CUA]). Determining COI is essential for selecting the most appropriate intervention option, and become able to economically furnish appropriate resources, especially in the presence of budgetary constraints or shrinking resources many healthcare environments are encountering [29]. In COI analysis, cost is split into direct – and – indirect costs. In DFDs, direct costs include medical expenditures (hospitalization, physician office visits, prescription medications, laboratory works, surgeries, hypoglycemic agents, insulins, disposables, devices, and supplies), and any other expenditures going directly toward caring for the condition. Indirect costs in COI of DFDs mostly refer to productivity losses due to morbidity and mortality borne by the individual, family, society, and the employer. Other indirect costs include cost of ambulatory or home care and rehabilitation. There is little research on the non-health related costs of diabetes or its complications, but targeted literature searches could identify some data that had been used to provide some estimates [30]. Computing for COI to analyze the desired economic consequence of DFDs, a clear discrimination between costs associated with diabetes itself and costs related to the assessed diabetic foot ulcer episode should be established. Naturally, no such distinction can always be made because often the same medication, laboratory test or procedure used in routine follow up of diabetes have to be utilized to evaluate the degree and severity of the DF problem studied. The same discrimination must be done to verify costs referable to studied DFD. This differentiation is especially important in the use of secondary data sources [31]. Such malpractice probably occurs in health care systems without a direct connection between the diagnosis and economic compensation but less likely to occurs in such systems where the reimbursement policy provides incentives for accurately coded diagnoses. Without careful COI assessment, no valid conclusions about the value of adopting certain technique for an effective and economic management of DFDs could have been made.

In Saudi Arabia (SA), the overall epidemiologic picture of diabetes is no departure from the global situation, if not worse. Like most oil-rich countries, leaving behind the physically demanding life of the desert for air-conditioned comfort, servants, and fast food and meat based dishes replacing fiber rich food, SA does struggle with obesity and diabetes. It is estimated that the prevalence of diabetes among adult Saudis has reached 17.5% - 23.7% [32,33], a rate that is one of the highest in the world. Within a changing economic environment, diabetes poses a progressive challenge stakeholders in Saudi Arabia are facing. The cost per person with diabetes in mounts up to $1,145.3. [33] Further, the number of undiagnosed diabetics had been estimated at 1.2243 million; adding another dimension to the challenge and raises resource issues. Afifi et al. (2015) [34] provide that 21.4% of all screened persons had random plasma glucose (RPG) ≥ 200 mg%, who were either uncontrolled diabetics (56% of high RPG and 12% of the study population) or undiagnosed (prediabetic) (44% of high RPG, and 9.4% of the study population). The participants had risk of high weight problems, where 43.6% were overweight and 41.8% were obese. In order to meet the growing populations’ demands for health care and ensure quality of provided services, the Council for Cooperative Health

Insurance (CCHI) was established by the Saudi government in 1999 [35]. The main role of CCHI was to regulate a health insurance strategy for the Saudi health care market. The implementation of a cooperative health insurance scheme was planned over three stages. In the first stage, cooperative health insurance was applied for non-Saudis and Saudis in the private sector, where the employers have to pay for health cover costs. In the second stage, the cooperative health insurance was to be applied for Saudis and non-Saudis working in the government sector, and in the third stage, health insurance yet to be applied to employees of all companies, domestic workers, and other groups, such as pilgrims. The introduction of the national insurance scheme was intended to decrease the financial burden due to the costs associated with providing health services free of charge to citizens. It also gives people more opportunity to choose the health services they require [36]. The scanty researches on DFDs in KSA have been undertaken in hospital settings [20]. On the other hand, the majority of other hospital-based researches on DFDs done elsewhere traditionally used quantitative measures of HRQOL, such as, the Nottingham health profile and the Diabetes QOL Measure [37]. From the societal perspective, too, it is therefore necessary to consider the economic impacts of DFDs, and identify interventions that can reduce the burden of these health problems. This study aimed to determine and analyze COI associated with DFD events treatment in the study population, in an attempt to explore and quantify the current economic burden of DFDs in Saudi Arabia. Findings from this work help healthcare decision-makers in prioritizing healthcare policies and interventions to improve diabetes and DF complications in the Saudi society.

2. METHODS

This study was conducted in Jeddah, a cosmopolitan city with over 3.4 million populations (13% of the total population of KSA) [38]. The private health care business in Jeddah contributes to around 42% of health services volume available for residents, who are obliged to including citizens and expatriates. The latter constitute a considerable proportion of workforce in Jeddah which business organizations target through providing attractive health insurance packages as one of the policies to retain their human resources. A group of health insurance providers in Jeddah were contacted and the research idea explained to them. Insurers were asked to provide de-identified data on type-2 diabetic subscribers during the period between 2012 and 2015. Diabetic patients who showed history of DFDs and were reimbursed for any DFD episode care during the study period were reviewed. Authorization to access anonymous patient data with specific restrictions and fulfilling confidentiality requirements on the part of the insurance agencies were fulfilled. Ethical permission from institutional review board of the Health Directorate of Jeddah was obtained. On our part, we have declared and acknowledged before the insurer that the obtained information would remain anonymous by de-personalizing any names and places in the transcriptions and ascertained that only grouped information would be disclosed at scientific and research settings. According to the study design, a subject is labeled as “type 2 diabetes mellitus” if she or he met the International Classification-9- Coding Manual (ICD-9-CM) criteria for type 2 diabetes diagnosis [39], where ICD-9: 250.00 refers to diabetes mellitus without mention of complication (the last pair of digits is left for complication coding; e.g., 250.70 is code to type 2 diabetes with PAD not stated as uncontrolled and 250.72 is code to diabetes with PAD stated uncontrolled; and so forth). (ICD-9-CM 250.80 is a billable code used to indicate a diagnosis on a reimbursement claim; however, it should only be used for claims with a date of service on or before September 30, 2015; yet for claims afterwards, ICD-10-CM code equivalent was used). According to ICD-9-CM, DFDs are coded as 250.00 which implies either diabetes with other specified manifestations, type 2 or unspecified type, or diabetes not stated as uncontrolled plus codes for systemic diseases compatible with the DFDs, [DFDs include ulcer of heel and mid foot, carbuncle and furuncle of foot, heel, toe (680.7), cellulitis and abscess of toe (681.1), cellulitis or abscess of foot (707.14), chronic osteomyelitis of ankle and foot (730.17), unspecified infection of bone of ankle and foot (730.97), atherosclerosis of the extremities with ulceration (440.23)]. Some insurers often used industry standard codes developed by “Clinical Coding & Schedule Development Group” (CCSD) (CCSD, http://www.ccsd.org.uk/), which contain codes for produces guidance to enable accurate coding of clinical activity in independent healthcare. Each ICD-9 diagnosis code of participants and its CCSD equivalent were matched for accurate admission to the study. Cost data were based on the reimbursement schedules provided by the insurer and according to the billing technique in action the time of the study. (Most insurers use a billing system which utilizes electronic submission of invoices for accurate reimbursement, which was also derived from the original International Classification of health Interventions coding system - ICHI) [39]. Patients were included in the study if they fulfilled ICD-9-CM type 2 diabetes diagnosis, had been enrolled with the insurer and developed and received medical and / or surgical care for any DFDs which had been reimbursed for in any fiscal year (FY) during of the study period. In case of more than one DFD episode encountered by the same patient, the most recent episode would be accounted. Patients should also be adults who stay in Jeddah as the place of residence the time of the study. Also all types of insurance policies were included, whether part of group insurance or individual plans.

The study sampling strategy was based on identifying a sample frame from which numbers of diabetic patients proportional to their total number on each insurance company's enrollee list could be selected. A frame of 3180 diabetic patient records was recognized. All those who developed DFD episodes during the study period were (229 insured) were included in the study. "All adult ages 18 and above were allowed to the study. Selected patients' consent for limited access to data related to the study was obtained. A predesigned proforma was used to administer the required information. The proforma includes five major fields, patient information, case and disease diagnosis and coding, clinical and laboratory findings, intervention and procedural actions, as well as direct costs data fields. Indirect costs, such as employee time or home care cost were not calculated, since they are not covered by the insurance plan. Likewise, extra medical charges paid at the patient's expense or outside the insurance plan were not included. At the beginning of this project, there was a desire to gather a full scope of demographic and clinical information to be used as potential risks of a hypothesized influence on the development of DFDs in the study participants. However, some restrictions involving socioeconomic status and comorbidities or other healthcare costs other than the searched DFD episode were not made available. For instance, not all patients' data, including other diabetes complications, were released. The rationale perhaps was to not jeopardize patients' confidentiality and the companies' billing privacy. In each insured's record, we learned that mainly the patients' clinical history, including procedures and services covered during enrollment, were only available. Some other clinical data not shared by the company were not included in record. On our part, it was well understood that assuring patient confidentiality was a top responsibility.

2.1 Study Variables

Demographic variables include age in years (y) (an interval ratio scale [IRS] variable), sex, and nationality (Saudi or non-Saudi). Clinical variables include type of DF complication, as well as the specific medical and/or surgical intervention advocated in four levels: conservative only, debridement, minor amputation, and major amputation. Compliance with treatment plan and commitment to scheduled follow up was also among input variables hypothesized to have had an influence upon tendency for being involved in invasive intervention, i.e., amputation events. Eventually, two sets of exposure variables were studied, demographic criteria and intervention level. The terms "risk factor," "risk," "input," "correlate," "dependent variable," all can be used interchangeably for these variables. Cost data, an IRS variable, indicates cost of illness per the DFD episode which had led to one of the treatment procedures described above. If more than one DFD episodes were encountered during the study period, the latest one would only be accounted. Also COI accounting was based on the following financial information: a) total direct medical costs, such as doctor's fee, outpatient visits, medicines, devices, hospital stay, and surgery, b) total non-medical costs, such as transportation, communications, room accommodation, and the likes, c) COI (total direct medical/surgical costs + subtotal direct medical/surgical costs, less deducible and copayment), (i.e., deductibles and copayment are not included in COI); all in Saudi Riyal (1SR=$0.267). While COI would be the ultimate outcome (dependent) variable to answer research questions, type of intervention could also become an "intermediary" outcome, since the intervention logically depends on other clinical and demographic criteria describing the study patients. Collected data were entered into a Microsoft system with adequate back up. Statistical analyses included both descriptive - and analytical statistics. For instance, IRS variables, such as COI and age would be described in terms of the mean ± standard deviation (SD) or the median ± interquartile range (IQR), where appropriate. Categorical variables, such as sex and nationality would be described in count (%). The statistical analysis plan was set forward so that the influence of a correlate may be tested both upon the type of intervention and COI. Intervention, in turn, may be tested against COI as an ultimate outcome. Analysis of the study correlates, e.g., the difference in the levels of COI among sex groups could be measured using student *t*- test, assuring the fulfillment of parametric techniques (PMT) assumptions; otherwise non-PMT alternatives would be used. Likewise, the influence of the type of intervention upon COI may be measured using one-way analysis of variance (ANOVA) test or the non-PMT alternative tests, where appropriate. Normality of the study's IRS data could be assessed using one-sample Kolmogorov-Smirnov (K-S) test. The association between any of the demographic categorical variables, such as nationality and intervention option could be assessed using Pearson's chi-square test (or Fisher's exact test, where appropriate). The statistical package for social sciences version 20 (SPSS Inc., Chicago, IL, USA) was used in the analysis. Our tolerable alpha error for rejecting a true null hypothesis was 0.05, and results with p-value <0.05 were considered significant.

3. RESULTS

As in Table 1, the mean subjects' age was 54.33±4.7, and median 55.04±3.7. The mean COI accounts 35,934.4±15,065.1, median 31,465.6 (IQR 16,354.5), 31, (minimum 41, maximum 72).

In Table 2, the majority (43.2%, n=99) of the study group had debridement as the first line of treatment for their DFD episode; then comes minor amputation (26.2, n= 60), major amputation (18.3%, n=42) and least occurring intervention was conservative treatment alone (12.2%, n=28 cases).

In Table 3, diabetics in the two age groups (<50y and ≥50y) slightly differed in the need for conservative treatment alone (7.9% and 4.3%, respectively). Those 50 or older were at greater risk for LEA, whether minor (24.4%) or major (17.5%) amputation. *(NB. The average diabetes disease duration in the study group as revealed from the reviewed data was 15.6y).* Among the non-amputation categories, diabetics ≥55were also more prone to debridement (35.8%) compared to the <55y counterparts (7.4%), *[Fisher's exact 27.5, p<0.0001].* All amputation episodes among Saudis diabetics significantly outnumbered the non-Saudi counterparts (23.6% vs. 2.6% minor amputation, and 14.4% vs. 3.9% major amputation, respectively). The same trend is observed in regard to debridement and conservative treatment (27.1% vs. 16.1%, and 8.3% vs. 3.9%, respectively), *(Fisher's exact 17.3, p 0.015).* (In another cross-tabulation

Table 1. Distribution of the study group by demographic criteria and COI

	Age (y)*	COI (SR)**
Mean ± SD	54.33±4.7	35934.4±15,065.1
Median ± IQR	55.04±3.7	31,465.6 (IQR 16354.5)
Range	31 (min. 41, max. 72)	141204 (min. 11,032; max. 152236)
		n (%)
Sex	Male	158 (68.9%)
	Female	71 (31.1%)
Nationality	Saudi	162 (71.0%)
	Non-Saudi	67 (29.0%)

** KS test age: Z=1.67, p=0.087. ** K-S COI: Z=1.35, p=0.11*

Table 2. Distribution of COI by selected intervention method

COI (SR)	Conservative treatment only	Debridement	Minor amputation	Major amputation
n (%)	28 (12.2%)	99 (43.2%)	60 (26.2%)	42 (18.3%)
Mean± SD	10278.8± 429.9	1727.6 ± 5317.5	35892.3 ± 5 9998	85921.0 ± 2333.1
Median (IQR)	10149.4 (IQR 877.8)	15323.0 (IQR 10285)	34828.0 (IQR 8683)	77133.0 (IQR 20203)
Range (min. – max.)	1098 (9859-10957)	16281 (11055 - 27364)	28289 (19801 - 48090)	83912 (68324 - 152236)

Table 3. Influence of some demographic and health trends on the selection of DFD intervention

Category		Intervention				Total	p-value
		Conservative only	Debridement	Minor amputation	Major amputation		
Age (year)[†]							p<0.0001*
<50y	n (%)	18 (7.9%)	17 (7.4%)	4 (1.7%)	2 (0.9%)	41 (17.9%)	
≥50y	n (n)	10 (4.3%)	82 (35.8%)	56 (24.4%)	40 (17.5%)	188 (82.1%)	
Total		28 (12.2%)	99 (43.2%)	60 (26.2%)	42 (18.3%)	229 (100)	
Nationality							
Saudi	n (%)	19 (8.3%)	62 (27.1%)	54 (23.6%)	33 (14.4%)	168 (73.4%)	p=0.015**
Non-Saudi	n (%)	9 (3.9%)	37 (16.1%)	6 (2.6%)	9 (3.9%)	61 (26.6%)	
Total		28 (12.2%)	99 (43.2%)	60 (26.2%)	42 (18.3%)	229 (100)	
Compliance with treatment							
Compliant	n (%)	18 (7.9)	59 (26.7)	18 (7.9)	12 (5.2)	107 (40.6)	P=0.04
Non-compliant	n (%)	10 (4.3)	40 (17.5)	42 (18.3)	30 (13.1)	122 (59.4)	
Total		28 (12.2)	99 (43.2)	60 (26.2)	42 (18.3)	229 (100)	

Fisher's exact 27.5* * Fisher's exact=17.3*

[†] *Average diabetes duration, as concluded from records was found to be 15.6y*

Table 4. The Relationship between Sex and COI

COI (SR)	Mean COI			Test statistic	p-value
	Male	Female	Difference		
By sex	32592.8±21749.9	32013.4±21375.7	579.4	00.16=(227df)*t*	0.88
By nationality	Saudi	Non-Saudi			
	34165.4±22151.7	12567.1±4673.2	21598.5	*t*(df 214.8) =9.7	<0.0001

to evaluate the influence of sex upon the type of intervention, no significant effect was found, Fisher's exact 0.276, p=0.683). Compliance with the prescribed treatment plan was also significantly associated with the type of intervention, for instance the need for severest invasive intervention, i.e., major amputation is significantly higher among noncompliant group compared to that among compliant group [30/229 (13.1%) vs. 12 (5.2%)], and he same trend was found in the need to resort to minor amputation [42 (18.3%) vs. 18 (7.9%), respectively], [Fisher's exact, p=0.004].

As in Table 4, the mean COI did not significantly differ by sex (mean COI male SR32,592.8 ±21749.9, mean COI female SR320,13.4 ± 21375.7) *[t(df 227) 0.16, p=0.88)].* The mean COI significantly differed between Saudi and non-Saudi groups. Saudis incur average SR341,65.4±22151.7, while non-Saudis incur SR12567.1±4673.2 [t(df 214.8) =9.7, p<0.0001] (Table 4). In a separate correlation analysis attempt, age and COI, both IRS, were significantly moderately correlated (*r*=0.67, p=0.003).

The mean COI increases significantly and gradually by the intensiveness of the intervention procedures (Table 5), conservative treatment alone costs SR103,29,4± 429.9; debridement SR169,63.5± 6117.5; minor amputation = SR367,64.4± 5998.1; and major amputation SR920,24.8± 25330.1 *[F(df 3, 225)= 426.9, p<0.0001].* A post-hoc test (Benferroni's) was also conducted to measure the "within-groups" difference in COI, whereas the vast majority of comparisons were significantly different.

4. DISCUSSION

In most developed countries, the annual incidence of foot ulcers amongst people with diabetes is about 2% [40]. In our work, the rate of DFU was up to 7.2% (229/3180) over four years of study duration, a figure more or less comparable to that could be accumulated over four years, worldwide (2% * 4 = 8%). According to Boulton, quarter of all people with diabetes at some point during their lifetime will develop ulcers in the skin of their feet. Factoring that our patients were only screened over 4-years of disease duration, and given that the average disease course in them was around 15.6 years (as drawn from the records), the frequency of DFDs, assuming the same standard of care and patient education mounts 28.1% (15.6y / 4y = 3.9; and 3.9 * 7.2 = 0.281; or 7.2% / 4 = 1.8%, and 1.8 *15.6 = 28.1), slightly exceeding the 25% international rate. While around 1% of diabetics suffer major LEA [40], our amputation rate was 3.2% (42/229=0.183 minor amputation + 60/229=0.262 major amputation; all = 102 out of total 3180 diabetics = 0.032). Also, the 18.3% - 26.2% amputation rate in this study conforms to what has been estimated locally in figures such as 15%-27% of diabetic cases by Alzahrani (2013) [20]. In most of our patients, LEA was one-time event during disease course; thereby the rate of LEA among them is almost three-times that seen elsewhere. Moreover, amputated diabetics in this study represent 44.5% of all diabetic foot cases (102/229=0.445), e.g., compared to 32.2% of patients with DFDs who had a form of amputation in a retrospective survey for the prevalence and risks of diabetic foot complications in Saudi adult populations by Al-Rubeaan et al. [41]. That the frequency of DFD episodes among our subjects was more or less in line with that worldwide [20,40], the prognosis tends to be on the worse side, in terms of higher LEA events. The cornerstone in mitigating diabetes complications is to control blood glucose level and guard against higher than optimum glucose levels by all means and under all circumstances. The longer the normalization of PG levels the farther postponement of the development of diabetic macrovasculopathy, neuropathy and other complications [42]. These pathologies endanger

Table 5. Difference in the mean COI of intervention options in the study group: ANOVA*

Intervention option	Mean COI	SD	SE	95% CI		Test statistic, p-value
				Lower	*Upper*	
Conservative only	10329.4	429.9	107.5	10049.6	10507.8	*F*(3; 295)
Debridement	16963.5	6117.5	521.4	16241.8	18310.1	=426.9
Minor amputation	36764.4	5998.1	654.4	34590.7	37194.0	p<0.0001
Major amputation	92024.8	25330.1	3888.3	78027.9	93815.4	

** ss: between groups 135408611124.667; within groups: 24951572173.667*
Mean square: between groups 24951572173.667; within groups: 105727000.736

foot tissue health and if not controlled DFDs of variable severities are precipitated [19,43].

Although many diabetics are at risk of developing DFU, the exact economic burden and COI estimate attributed to DFU are lacking [20, 44]. We first found that both age and having Saudi nationality were risks for a severer diabetic foot ulcer prognosis, sex was not. In Saudi Arabia, Alrubean and collaborates (2015), too, found that age, male sex, and diabetes duration were risk factors for worse diagnoses [41]. Alrubean et al. work was based on reviewing a newly established Saudi National Diabetes Registry (SNDR), whereas it was reported that only a total 2,071 DFD cases were registered with SNDR, and 32.2% of those who sustained worst diagnoses (ulcer and gangrene) had major amputation. The amputation frequency in our study is 1.4-times that of Alrubean and collaborates' (44.5%/32.2%=1.38); and this gives us a reason to be concerned about such amputation rate in a population which is fully covered and supposedly has access to good medical care. Alrubean et al. finding that 2071 subjects had DFUs through twelve years of study (2000 - 2012) in turn raises a greater concern about DFDs situation in SA. Assuming a least estimate of 3.3% of DFDs in KSA, as in Alzahrani (2013) [20], this proportion should account to not less than 100,000 cases, (considering 3.4 million with diabetes in KSA [33] and that 90% of them are type 2) [45], (3.4*0.9=3.06 million type 2 DM; and 100,000 / 3.06m = 0.0326 or 3.3%). The difference in DFDs prevalence between the two reports warrants further inquiry about the true reason for under-reporting diabetes disorders and the inconsistency in administering DFDs incidents in the SNDR. In Saudi Arabia, progressive medical, strategic and administrative advances in health services have been widely envisioned [36]. Therefore, the discouraging DFDs outcome reported in our study fails our expectation of a better outcome in such insured population and driven by a prosperous market economy the time of the study, such as that in Jeddah. Many factors could be incriminated in our attempt to understand the mismatch between this unfavorable health outcome and the leveraged financial and health system inputs available.

Regional and international diabetes research critics find studies addressing the prevalence and risks of DFDs in KSA as scarce [20,36,41], in agreement with our instinct with this regard. Instead, the prevalence of diabetes itself in Saudis compared with other nations has been addressed more extensively [32,34,46]. Diabetes in KSA reached 23.7% [36], highest not only in MENA zone but in globally and it is prone to grow to astronomical numbers if the Saudi diet style and physical inactivity persist intervention plan has been enforced. In diabetes, early detection of clinical and pathological risks for diabetic foot ulceration, namely vasculopathy and neuropathy of the foot, is critical [8]. These pathologies frequently overlap in the same DFD episode and progress to a resistant ulcer and then amputation [41]. Poor compliance with the prescribed treatment or reluctance to adhere to the follow up plans has been associated with involvement into severer prognosis and higher incidence of amputation episodes. A radical strategy to handle the diabetes problem in Saudi Arabia should rest on prevention, early detection of prediabetes and uncontrolled diabetes cases and continuous monitoring of A1c in known diabetics [34]. Especially the high risk, diabetics should be given specific consideration at family medicine and primary healthcare setting. There should be also an emphasis on a combined screening strategy for high risk groups, including the obese, less served communities, and the low socioeconomic class. Even the high socioeconomic class should be considered in risk detection of diabetes. All socioeconomic classes have reasons to an exaggerated diabetes opportunity. The unfortunates lack access to health care both in quantity and quality. The less educated may not have the enthusiasm for health education and realizing its role in preventing chronic diseases which impact health and QOL [8,13,19,20]. The rich are often intimidated by easy life and often unhealthy diet, as well as technologies which bring the plenty of life utilities at the fingertips and persuade physical inactivity. Reportedly, the cost per person with diabetes in Saudi Arabia mounts up to $1,145.3 [33]. This implies that the Saudi society spends over $15 billion on diabetes ($1145.3 * 3.4 million estimated diabetics), while the outcome, e.g., 27.9% - 44% prediabetes prevalence [34,46], and 18.3% - 26.2% amputation among diabetics, as in this study, does not live up to that expected from the investment. The median COI for DFD care in this study was SR31,465.6 (IQR 16,354.5). Data from a recent sample-based study on the cost of diabetic foot illnesses in Saudi Arabia [20] show that the median COI totaled SR12,819.5. The median COI in Alzahrani study [20] is less than half ours. On the other hand, both Alzahrani's and this study share some common clinical approach criteria. For instance, the broad clinical intervention categories were almost identical (conservative treatment alone, debridement, minor amputation, major amputation). Studies elsewhere on DFDs also tend to use similar intervention classification [24]. According to Alzahrani study design, recruitment was limited to DFD patients upon a single hospital admission to receive inpatient care for their stressing DFD condition. In practice, however, patients with DFDs tend to require more frequent emergency visits and outpatient appointments, and probably other follow up procedures in-between visits [24]. Therefore, larger-scale costing studies for DFDs not only including the immediate DFD episode cost but other costs are required [24]. Further, indirect cost items would preferably be calculated. However the estimation of these costs is not always possible, especially in the presence of obstacles that limit the allocation of resources for a comprehensive COI study. The frequency of debridement intervention in Alzahrani study and ours was highest among all diabetic foot procedures (48.8% and 43.2%, respectively). Findings from western economic research report variable costs for DFD care. The trend was that LEA usually costs higher than non-surgical care [26]. The median cost for LEA in Australia was A$12,485, (range 6,037-24,415) [26], compared to $9,287.5– $20,568.8 median COI equivalent for amputation (all types) in our study. Highest among all, $32,129 was median cost in admission for LEA in USA [47]. The differences in study designs, procedures, length of hospital stay, as well as the variability in health benefits and billing systems alongside with the variability in each country's economics and living expenses all could cause the variability in COI of DFDs care in the two countries. As in the type of intervention analysis, age and nationality were risks for incremental COI. Comparable results have been reported by other diabetic foot ulceration costing studies [41]. Typically, diabetes complications develop after many years (10–20y), but may be the first symptom in those who have otherwise not received a diagnosis before that time. As such, older diabetics are at greater risk of suffering a complicated disease [48,49].

5. STRENGTHS AND LIMITATIONS

This work has a number of strengths adding to the validity and reliability of the obtained findings. Selecting DFD as the hypothesis of interest enabled conducting a larger number of comparisons and tackling DFDs from the economic side, a vision that is barely addressed by local or regional research. On the other hand, some limitations mostly related to access to patient data were encountered, such as lack of full medical and comorbidity history and ongoing healthcare expenditures of the study cohort. Also, we were not permitted to track or interview patients whereas other economic aspects such as out-of pocket and indirect costs could have been addressed in the analysis.

6. CONCLUSION

Overall, despite good coverage and access to health care, the incidence of amputation among Saudi diabetics is alarming. This warrants developing more efficient follow up policy for diabetics in general; and DFD patients in particular. Obese diabetics and those with CVD are worth closer monitoring. Keeping diabetic patients under continuous glycemic control can delay the occurrence of ischemic vascular and neurological complications, and hence obviate serious implications upon the patient's foot wellbeing. A preventive approach both to minimize the number of new diabetics and create an unfavorable environment for developing complications is stressing. Importantly, too is that any prevention policy should include methods to enhance patient compliance with DFD management and scheduled follow up plan in order to minimize the likelihood of the need for amputation. Improving the primary prevention programs, adopting a multidisciplinary collaboration in delivering holistic healthcare service packaging is critical for alleviating diabetes problems burdening the Saudi community and the nation's economy. Future large scale research addressing indirect costs, moral hazard, and impaired QOL due to loosing limbs to diabetes is warranted particularly within populations with an exceptionally high rate of diabetes, such as Saudi Arabia.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. World health Organization (WHO). Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus (WHO/NCD/NCS/99.2). Geneva: WHO; 1999.

Available:http://apps.who.int/iris/bitstream/10665/66040/1/WHO_NCD_NCS_99.2.pdf
2. World Health organization (WHO). Diabetes fact sheet N°312". WHO; 2013. Available:https://web.archive.org/web/20130826174444/http://www.who.int/mediacentre/factsheets/fs312/en/
3. Young MJ, Cavanagh PR, Thomas G. The effect of callous removal on dynamic plantar foot pressure in diabetic patients. Diabetic Medicine. 1992;9:75–77.
4. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the global burden of disease study 2010. The Lancet. 2012;380(9859):2163–96. DOI:10.1016/S0140-6736(12)61729-2.
5. World Health Organization (WHO). Media Center. Diabetes. "The top 10 causes of death Fact sheet. N°310"; 2014. Available:http://www.who.int/mediacentre/factsheets/fs310/en/
6. World Health Organization (WHO). Global report on diabetes; 2016. Available:http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf
7. American Diabetes Association (ADA). Diagnosis and classification of diabetes mellitus. Diabetes Care; 2004;27(suppl 1):s5-s10. Available:http://dx.doi.org/10.2337/diacare.27.2007.S5
8. American Diabetes Association (ADA). American Diabetes Association's "Standards of Medical Care in Diabetes" Summary of Revisions Diabetes Care, 2015;38(Suppl. 1):S4. DOI: 10.2337/dc15-S003.
9. World Health Organization (WHO). Diabetes programme. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. Report of a WHO/IDF consultation; 2006. Available:http://www.who.int/diabetes/publications/diagnosis_diabetes2006/en/
10. Selven E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. New England Journal of Medicine, 2010;362(9):800–11. DOI:10.1056/NEJMoa0908359.PMC 2872990. Saudi Arabia Population Clock. Available:http://countrymeters.info/en/Saudi_Arabia
11. Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, Goyder E, et al. Screening for type 2 diabetes: Literature review and economic modeling. Health Technology Assessment. 2007;11(17). Available:www.hta.ac.uk/execsumm/summ1117.htm
12. Global Burden Disease Risk Factors Collaborators (GBD). Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the GBD Study 2013. The Lancet. 2015;386(10010): 2287–323. DOI: http://dx.doi.org/10.1016/S0140-6736(15)00128-2
13. Moxey PW, Gogalniceanu P, Hinchliffe RJ, Loftus IM, Jones KJ, Thompson MM, et al. Lower extremity amputations – A review of global variability in incidence. Diabetic Medicine. 2011;28(10):1144–1153.
14. International Diabetes Federation (IDF). Diabetes atlas, (6th ed). 2013;7. ISBN 2930229853.
15. Non-Communicable Disease Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4*4 million participants. The Lancet. 2007;387:1513–1530. DOI: http://dx.doi.org/10.1016/S0140-6736(16)00618-8.
16. Reiber GE, Lipsky BA, Gibbons GW. The burden of diabetic foot ulcers. American Journal of Surgery, 1998;176(suppl 2A):5S-10S. Available:http://www.ncbi.nlm.nih.gov/pubmed/9777967
17. Green MF, Aliabadi PTZ, Green BT. Diabetic foot: Evaluation and management. Southern Medical Journal. 2002;95(1):95-101.
18. Young MJ, Cavanagh PR, Thomas G. The effect of callous removal on dynamic plantar foot pressure in diabetic patients. Diabetic Medicine. 1992;9:75–77.
19. Tashkandi WA, Badri MM, Badawood SM, Ghandoura NA, Alzahrani HA. Lower limb amputation among diabetics in three major hospitals in Jeddah, Saudi Arabia. Saudi Medical Journal. 2011;18: 23–35.
20. Alzahrani HA. The direct cost of diabetic foot management in some of private hospitals in Jeddah, Saudi Arabia. International Journal of Diabetes in

Developing Countries. 2013;33(1):34–39. DOI: 10.1007/s13410-012-0107-x.
21. Al-Tawfiq JA, Johndrow JA. Presentation and outcome of diabetic foot ulcers in Saudi Arabian patients. Advances in Skin Wound Care. 2009;22:119–21.
22. Roglic G. WHO global report on diabetes. A summary review article. 2016;1(1):3-8. Available:http://www.ijncd.org/article.asp?issn=WKMP-0120;year=2016;volume=1;issue=1;spage=3;epage=8;aulast=Roglic
23. Driver VR, Fabbi M, Lavery LA, Gibbons G. The costs of diabetic foot: The economic case for the limb salvage team. Journal of Vascular Surgery. 2011;52(3 Suppl):17S–22S. Available:http://www.ncbi.nlm.nih.gov/pubmed/20804928
24. Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. The Lancet. 2005;366:1719–24.
25. Lamri L, Gripiotis S, Ferrario A. Diabetes in Algeria and challenges for health policy: A literature review of prevalence, cost, management and outcomes of diabetes and its complications. Global Health. 2014;10:11. DOI: 10.1186/1744-8603-10-11
26. Davis WA, Norman PE, Bruce DG, Davis TM. Predictors. Consequences and costs of diabetes-related lower extremity amputation complicating type 2 diabetes: The Fremantle diabetes study. Diabetologia. 2006;6(49):2634–41.
27. American Diabetes Association (ADA). Diabetes Care. Summary of Revisions for the 2010 Clinical Practice Recommendations". Diabetes Care. 2010;33(Supplement 1):S3-3.
28. Jefferson T, Demicheli V, Mugford M. Cost-of-illness studies, elementary economic evaluation in health care. 2nd ed. London: British medical Journal Publishing Group. 2000;17–29.
29. Jo C. Cost-of-illness studies: concepts, scopes, and methods. Clin Mol Hepatol. 2014;20(4):327–337. DOI: 10.3350/cmh.2014.20.4.327.
30. Hex N, Bartlett C, Wright D, Taylor M, Varley D. Health Economics Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. York Health Economics Consortium Ltd, University of York, York, UK; 2012. DOI: 10.1111/j.1464-5491.2012.03698 x.
31. Masson EA, MacFarlane IA, Power E, Wallymahmed M. An audit of the management and outcome of hospital inpatients with diabetes: resource planning implications for diabetes care team. Diabetes Medicine. 2009;9:753-5.
32. Alwakeel JS, Al-Suwaida A, Isnani AC, Al-Harbi A, Alam A. Concomitant macro and micro-vascular complications in Diabetic nephropathy. Saudi Journal of Kidney Disease Transplantation. 2009;20:402–9.
33. International Diabetes Federation (IDF). Middle East and North Africa. Diabetes in Saudi Arabia; 2015. Available:http://www.idf.org/membership/mena/saudi-arabia
34. Afifi R, Omar S, El Raggal A. A community screening plan for the prevalence of some chronic diseases in specified adult populations: Pre-diabetes and diabetes mellitus. International Journal of Diabetes in Developing Countries. 2015;35(3):149-156.
35. Council of Health Services. Vision and tasks of the Council of Health Services in Saudi Arabia. Available:http://www.cchi.gov.sa/en/InsuranceCompanies/Pages/Companies.aspx?PageIndex=2
36. Walston S, Al-Harbi Y, Al-Omar B. The changing face of healthcare in Saudi Arabia. Annals of Saudi Medicine. 2008;28:243–250.
37. Keinanen-Kiukaanniemi S, Ohinmaa A, Pajunpaa H, Koivukangas P. Health related quality of life in diabetic patients measured by the Nottingham Health Profile. Diabet Med. 1996;13(4):382-8.
38. Saudi Arabia Population Clock. Available:http://countrymeters.info/en/Saudi_Arabia
39. New International Classification-9- Coding Manual (ICD-9-CM). ICD-9-CM official guidelines for coding and reporting effective October 1, 2011. Available:https://www.cdc.gov/nchs/data/icd/icd9cm_guidelines_2011.pdf
40. Boulton A. The diabetic foot: epidemiology, risk factors and the status of care Diabetes Voice, vol. 50 Special Issue; 2005. Available:https://www.idf.org/sites/default/files/attachments/article_368_en.pdf
41. Al-Rubeaan KH, Al Derwish M, Ouizi S, Youssef AM, Subhani SN, Ibrahim HM, et

al. Diabetic foot complications and their risk factors from a large retrospective cohort study. PLoS One. 2015;10(5): e0124446.
DOI: 10.1371/journal.pone.0124446
42. Hammes HP. Pathophysiological mechanisms of diabetic angiopathy. Journal of Diabetes Complications. 2003;17(2 Suppl): 16-9.
43. Kalish J, Hamdan A. Management of diabetic foot problems. J Vasc Surg. 2010;51:476–86.
44. Al-Maskari F, El-Sadig M, Nagelkerke N. Assessment of the direct medical costs of diabetes mellitus and its complications in the United Arab Emirates. BMC Public Health. 2010;10:679.
45. International Diabetes Federation (IDF). Annual report; 2014.
Available:http://www.idf.org/sites/default/files/IDF-2014-Annual-Report-final.pdf
46. Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, Al-Harthi SS, Arafah MR, Khalil MZ, et al. Diabetes mellitus in Saudi Arabia. Saudi Medical Journal. 2004;25:1603–1610.
47. Peacock JM, Keo HH, Duval S, Baumgartner I, Oldenburg NC, Jaff MR, et al. The incidence and health economic burden of ischemic amputation in Minnesota. 2011;2005–2008. Preventing Chronic Disease, 8, A141.
Available:http://www.ncbi.nlm.nih.gov/pubmed/22005634
48. Abolfotouh MA, Alfaifi SA, Al-Gannas AS. Risk factors of diabetic foot in central. Saudi Arabia. Saudi Medical Journal. 2011;32:708–713.
49. Reiber GE, Lipsky BA, Gibbons GW. The burden of diabetic footulcers. American Journal of Surgery. 1998;176(suppl 2A):5S-10S.
Available:http://www.ncbi.nlm.nih.gov/pubmed/9777967

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/18124