ORIGINAL RESEARCH PAPER

Volume-6 | Issue-11 | November-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PREVALENCE AND RISK FACTORS FOR DIABETIC FOOT LOWER LIMB AMPUTATION: A HOSPITAL BASED CASE CONTROL STUDY

General Surgery

Dr Anurag Khare MS Surgery Assistant Professor, Department of General Surgery, Career Institute of Medical Sciences and Hospital, Lucknow.

Dr Vijai Kumar Misra* MS Surgery Assistant Professor, Department of General Surgery, Career Institute of Medical Sciences and Hospital, Lucknow. *Corresponding Author

ABSTRACT

Background: Diabetic Foot Ulcer occurs as a diabetic complication and involves a multi factorial pathogenesis including peripheral neuropathy as the primary causal factor, together with variable contribution from peripheral vascular disease (PVD), repetitive trauma, and superimposing foot infection. Infected DFU is a major cause of prolonged hospital admission and contributes over 90% of non traumatic lower limb amputations (LLAs), which is more than a million amputations/year.

Objectives: The aim of the study was to evaluate the prevalence of and risk factors for lower limb amputation in a specialist foot hospital-based setting.

Material and Methods: A retrospective quantitative study was conducted, using clinical and biochemical profiles of diabetic foot patients attending the High Risk Foot Clinic at Career Institute of Medical Sciences and Hospital, between January 1, 2016, and December 31, 2016.

Results: The total study sample included 110 subjects, comprising 80 males and 30 females with M: F ratio of 2.6 : 1. The average age of the cohort was 63.4 years ± 14.1 years [CI 90.98–65.89]. Lower limb amputation was identified as a common and significant outcome ($n = 40$), occurring in 35%, more commonly amongst the indigenous population (56.5% versus 29.2%; $p = 0.94$, OR 0.94). Risk factors most closely associated with amputation included diabetic retinopathy ($p = 0.00$, OR 4.4), coronary artery bypass graft (CABG) surgery ($p = 0.01$, OR 4.1), Charcot's arthropathy ($p = 0.01$, OR 2.9), and Indigenous ethnicity ($p = 0.01$, OR 3.4).

Conclusion: Lower limb amputation is a common outcome and linked to ethnicity and neurovascular diabetic complications amongst subjects with diabetic foot ulcer. Further research is needed to identify why risk of lower limb amputation seems to differ according to ethnicity.

KEYWORDS

Diabetic Foot Ulcer, Lower Limb Amputation, Charcot's arthropathy

Introduction:

Diabetes and the diabetic foot ulcer (DFU) have made their mark in society, with the prevalence of diabetes being four times higher than all cancers combined [1]. Increased life expectancies have contributed significantly to this exponential rise, with diabetes now contributing to 9% of global mortality, equating to 4 million deaths per year [2, 3]. DFU occurs as a diabetic complication and involves a multifactorial pathogenesis including peripheral neuropathy as the primary causal factor, together with variable contribution from peripheral vascular disease (PVD), repetitive trauma, and superimposing foot infection [4, 5]. Infected DFU is a major cause of prolonged hospital admission and contributes over 90% of nontraumatic lower limb amputations (LLAs) [6, 7], which is more than a million amputations/year [8–10]. We have seen a 50% 5-year mortality rate amongst diabetic amputees [11–14].

The progressive rise of diabetes is likely to pose a significant burden on future society leading to an associated increase in diabetic amputations [15, 16]. Despite previous alert to the importance of early detection and management, prevention practices remain poor, with inconsistent patient follow-up and management compliance [17, 18]. As a result, subjects with DFU maintain poorer quality of life, with higher baseline depression rate, and 5-year mortality rates of up to 74% [19]. Existing studies have identified presence of microvascular complications as contributing factors to poor DFU outcomes [20]. Furthermore there is no current data on the burden of either amputation or macrovascular outcomes amongst subjects with DFU in clinic setting in India which is home to amongst other population at risk of diabetes.

Aim and Objectives

This study endeavoured to bridge the current knowledge gaps, with particular focus on determining prevalence of and identifying risk factors of limb amputations amongst patients with DFU attending a typical Indian regional diabetes foot clinic.

Material and Methods

Eligibility Criteria. All patients attending the High Risk Foot Clinic (HRFC) at Career Institute of Medical Sciences and Hospital between January 1, 2016, and December 31, 2016, were included in the study. Patients 18 years of age and over with a confirmed diagnosis of either type 1 or type 2 diabetes and coexisting DFU were included. Subjects under the age of 18 and those with nondiabetic foot ulcers (e.g., traumarelated, vasculitic, and neoplastic ulcers) were excluded from the study. Subjects who attended the clinic for other management purposes (e.g., podiatry reviews, nail pathology, and education about prevention) were also excluded.

Data Extraction. There were two main processes involved in data extraction, including gathering of clinical and biochemical data from patient profile. A retrospective chart audit was initially performed, focusing on the correspondence and outpatient attendance sections. The HRFC pro forma sheet was then used to collect information regarding the onset, duration, outcome, and type of ulcer defined as ischaemic or nonischaemic based on University of Texas Wound Classification System [21]. Furthermore, clinical information on the diagnosis and management of diabetes, coexisting macrovascular and microvascular complications, and medication lists of the subjects was recorded. We also obtained biochemical data using the hospital's pathology system. Main parameters gathered included results of full blood count, urea and electrolyte studies, lipid profiles, Hba1c levels, and serum calcium, phosphate, and C-reactive protein levels. Average figures over the three-year period were calculated and included.

Data Analysis. SPSS software was utilised to perform data analysis. Basic descriptive and frequency analyses of the study sample were implemented to obtain demographic characteristics, period prevalence of clinical outcomes and diabetic complications, and mean age of the study population. In addition, a combination of nonparametric and chi-squared analyses was performed to identify differences in scaled data and rank risk factors associated with amputation, respectively. value of less than 0.05 was considered statistically significant and together with odds ratios and confidence intervals was included in our results. All significant values were entered into binary logistic regression analysis and correction for multiple regression logistic testing was then conducted and factored in as part of our final results.

Results

A total of 110 subjects were included in the analysis of this study, with 72.7% being male ($n = 80$) and 27.3% female ($n = 30$) (refer to Table 1). The mean age of the study cohort was 63.4 ± 14.1 years [CI 60.98–65.89]. The Indigenous cohort comprised 31.8% ($n = 35$). Patients were categorised according to comparison groups of ischaemic ($n = 50$) and non ischaemic ($n = 60$) ulcers. The period prevalence of amputation within the study sample was 36.6% ($n = 40$), with 35.1% belonging to ischaemic ($n = 18$) and 33.3% non ischaemic ($n = 22$)

cohorts. Amputation occurred more commonly at a rate of 56.5% amongst the Indigenous subjects, in comparison with 29.2% in the non- Indigenous group, with a significant difference amongst the ischaemic and non ischaemic ulcer cohorts (69.2% versus 30.8%). The mean age of amputation of 62.6 ± 12.5 years [CI 55.09–70.14] amongst the Indigenous cohort was similar to their non-Indigenous counterparts, mean age of 62.0 ± 11.5 years [CI 57.81–66.25]. Amputation rates were much higher amongst patients with PVD.

Table 1: Basic study characteristic and prevalence of adverse outcomes

Characters	Results			
Age	63.43 years ± 14.07 years [CI 60.98–65.89]			
Sex	Males (*n* = 80; 62.8%); females (*n* = 30; 37.2%)			
Religion	Indigenous (*n* = 35; 31.8%); non-Indigenous (*n* = 75; 68.2%)			
Type of diabetes	Type 1 (*n* = 25; 22.7%); type 2 (*n* = 85; 77.3%)			
Type of ulcer	Ischaemic (*n* = 50; 45.4%); nonischaemic (*n* = 60; 54.6%)			
Clinical outcome	**Total study sample**	**Ischemic ulcer cohort**	**Non ischemic ulcer cohort**	**P value**
Amputation	40 (36.6%)	18	22	P=0.84
Minor amputation	35 (31.8%)	15	20	P=0.50
Major amputation	10 (9.0%)	05	05	P=0.50
Ischemic heart disease	60 (54.5%)	35	25	P=0.15
Acute myocardial infarction	25 (22.7%)	20	05	P=0.18
Cerebrovascular accident	20 (18.8%)	12	08	P=0.19
Chronic kidney disease	50 (45.4%)	27	23	P=0.20
Peripheral vascular disease	90 (81.8%)	40	50	P=0.33

Table 2: Risk factors associated with lower limb amputation in study population

Risk factors	P value
Coronary artery bypass graft surgery	$p = 0.01$, 7.5 [1.81–30.76]
Indigenous ethnicity	$p = 0.02$, 3.3 [1.17–9.16]
Charcot's arthropathy	$p = 0.01$, 3.6 [1.38–9.29]
Retinopathy	$p = 0.00$, 5.2 [2.15–12.75]

Males got amputated more frequently (59.1%) compared to females (40.9%), although the mean age of male and female amputees differed minimally at 61.0 years and 63.9 years, respectively. Prevalence of ischaemic heart disease (IHD), acute myocardial infarcts (AMI), CABG surgery, strokes, and dialysis was significantly higher amongst ischaemic ulcer patients, occurring at overall rates of 54.4%, 26.3%, 15.8%, 19.3%, and 7.0%, respectively. Chisquared analysis identified diabetic retinopathy (p = 0.00, OR 4.4 [2.15–12.75]), Indigenous background ($p = 0.01$, OR 3.1 [1.17–9.16]), Charcot's arthropathy ($p = 0.01$,OR 2.9 [1.38– 9.29]), longer diabetes duration, defined as 15 years or longer ($p = 0.03$, 2.2 [1.00–4.86]), dyslipidaemia ($p = 0.04$, 3.4 [0.94–12.38]), neuropathy ($p = 0.03$, 3.3 [1.05–10.26]), PVD ($p = 0.04$, 2.6 [1.03–6.55]), and CABG surgery ($p = 0.01$, OR 4.1 [1.81–30.76]) to be significantly associated with increased risk of amputation, amongst others (refer to Table 3). Binary logistic regression analyses identified retinopathy, CABG surgery, Charcot's arthropathy, and Indigenous background as the most significant risk factors for amputation (refer to Table 4). Clinical parameters that fell short of statistical significance include smoking history ($p = 0.49$), dialysis ($p = 0.62$), diabetes type (p = 0.46), male sex (p = 0.53), multiple-ulcer history ($p = 0.15$), previous history of DFUs ($p = 0.06$), and ulcer type ($p = 0.84$) and grade ($p = 0.93$).

Discussion

In this hospital based case control study we have demonstrated prevalence of amputation in our study population to be 36.6%, a figure that is considerably higher in comparison with others' findings of 15.4% to 21.4% [22, 23]. On the other hand our report conforms to Miner and Kirsner and Amogne et al. report of higher rate of LLA in their respective diabetic foot clinic populations [13, 24]. The high prevalence might be related to inclusion of the population at the highest risk of the disease and its complications [25]. Furthermore, whilst there was a marginal difference in amputation between ischaemic and nonischaemic cohorts in the overall group, amputations related to ischaemic ulcers were more than double amongst the Indigenous subgroup. Essentially, the prevalence of amputation amongst our subjects stood at comparatively higher numbers and occurred predominantly amongst Indigenous subjects with ischaemic ulcers.

We identified numerous clinical factors that correlate with higher amputation risk, most in keeping with previous literature, in addition to new, undocumented parameters. Themost significant contributing factors were diabetic retinopathy, CABG surgery, Charcot's foot, and Indigenous ethnicity. Whilst Ndip et al. found no association with retinopathy but reported a 2-3-fold amputation risk amongst patients with diabetic neuropathy [26], results that are consistent with ours, which isolate neuropathy and dyslipidaemia as significant risk factors for amputation. We identified PVDwith increased risk of adverse outcome, also supported by current literature, which labels it as a causal factor for amputation and mortality amongst diabetics [27–30]. We have additionally extended existing knowledge by highlighting CABG surgery as a novel risk factor for amputation, which supports the role of both microvascular and macrovascular disease as significant risk factors for LLA in subjects with diabetic foot ulcer.

Our results identified other risk factors of LLA in subjects with DFU including Charcot's arthropathy, a history of osteomyelitis, and severity of foot infection or cellulitis requiring antibiotic treatment.Our result was in keeping with the previously reported 30% rate of amputation in subjects with Charcot's arthropathy, placing DFU patients at a 12 times higher lifetime risk of amputation [31, 32]. Similarly, in keeping with our findings, Wukich et al. have linked history of cellulitis and moderate-to-severe foot infection to amputation [33]. There is notably no current evidence suggesting use of antibiotics to prevent infections in subjects with DFU at risk of LLA in spite of our findings of antibiotics use preceding amputation.

Conclusion

We have documented high prevalence of lower limb amputation in our study population. In keeping with our hypothesis, the ischaemic ulcer cohort demonstrated higher rates of adverse clinical outcomes, including IHD, strokes, and renal disease. Numerous known and novel demographic and clinical risk factors were coupled with amputation, the most significant of them being Indigenous ethnicity, diabetic retinopathy, Charcot's arthropathy, and CABG surgery. Whilst there were no significant differences in amputation prevalence between the ischaemic and non ischaemic groups in the overall cohort, Indigenous subjects with ischaemic ulcers were amputated much more frequently. Extended research in the local area is encouraged to study factors leading to selectively higher amputation rate in the Indigenous population. We have made a huge development in identifying predisposing characteristics amongst DF patients, but our knowledge is not yet comprehensive to enable us to prevent limb amputation in the high risk diabetic population.

Limitations

As it is a single centre study with a relatively small study population, results cannot be generalized to the entire population.

Acknowledgement

We extend our sincere thanks to Dr.Abhishek Arun (MD) for his assistance in medical writing. We are also thankful to junior doctors and staff of Surgery department Career Institute of Medical Sciences and Hospital, Lucknow. Special thanks to everyone who participated in the study.

References

[1] A. D. McInnes, "Diabetic foot disease in the United Kingdom: about time to put feet first," Journal of Foot and Ankle Research, vol. 5, no. 1, article 26, 2012.

[2] J. E. Shaw, R. A. Sicree, and P. Z. Zimmet, "Global estimates of the prevalence of diabetes for 2010 and 2030," Diabetes Research and Clinical Practice, vol. 87, no. 1, pp. 4–14, 2010.

[3] D. R. Whiting, L. Guariguata, C.Weil, and J. Shaw, "IDF Diabetes Atlas: global estimates of the prevalence of diabetes for 2011 and 2030," Diabetes Research and Clinical Practice, vol. 94, no. 3, pp. 311–321, 2011.

[4] A. J. M. Boulton, "The pathway to foot ulceration in diabetes,"Medical Clinics of North America, vol. 97, no. 5, pp. 775–790, 2013.
[5] L. A. Lavery, N. A. Hunt, J. LaFontaine, C. L. Baxter, A. Ndip, and A. J. M. Boulton, "Diabetic foot prevention: a neglected opportunity in high-risk patients," Diabetes Care, vol. 33, no. 7, pp. 1460–1462, 2010.
[6] S. Tiwari, D. D. Pratyush, A. Dwivedi, S. K. Gupta, M. Rai, and S. K. Singh, "Microbiological and clinical characteristics of diabetic foot infections in northern India," Journal of Infection in Developing Countries, vol. 6, no. 4, pp. 329–332, 2012.
[7] National Amputee Statistical Database (NASDAB), National Amputee Statistical Database Annual Report 2004/2005, UK: NASDAB, 2005, http://www.limbless-statistics.org/.
[8] B. Peter-Riesch, "The diabetic foot: the never-ending challenge," Endocrine Development, vol. 31, pp. 108–134, 2016.
[9] S. C. Wu, V. R. Driver, J. S. Wrobel, and D. G. Armstrong, "Foot ulcers in the diabetic patient, prevention and treatment," Vascular Health and Risk Management, vol. 3, no. 1, pp. 65–76, 2007.
[10] M. Neidrauer, L. Zubkov, M. S.Weingarten, K. Pourrezaei, and E. S. Papazoglou, "Near infrared wound monitor helps clinical assessment of diabetic foot ulcers," Journal of Diabetes Science and Technology, vol. 4, no. 4, pp. 792–798, 2010.
[11] S. Schirmer, R.-G. Ritter, and H. Fansa, "Vascular surgery, microsurgery and supramicrosurgery for treatment of chronic diabetic foot ulcers to prevent amputations," PLoS ONE, vol. 8, no. 9, Article ID e74704, 2013.
[12] E. P. Weledji and P. Fokam, "Treatment of the diabetic foot—to amputate or not?" BMC Surgery, vol. 14, article 83, 2014.
[13] A. Miner and R. S. Kirsner, "Diabetic control affects healing rates in neuropathic and vasculopathic patients," The Journal of Investigative Dermatology, vol. 131, no. 10, p. 1962, 2011.
[14] J. M. Robbins, G. Strauss, D. Aron, J. Long, J. Kuba, and Y. Kaplan, "Mortality rates and diabetic foot ulcers: is it time to communicate mortality risk to patients with diabetic foot ulceration?" Journal of the American Podiatric Medical Association, vol. 98, no. 6, pp. 489–493, 2008.
[15] T. H. Kim, K. H. Chun, H. J. Kim et al., "Direct medical costs for patients with type 2 diabetes and related complications: a prospective cohort study based on the korean national diabetes program," Journal of Korean Medical Science, vol. 27, no. 8, pp. 876–882, 2012.
[16] Z. Liu, C. Fu, W. Wang, and B. Xu, "Prevalence of chronic complications of type 2 diabetes mellitus in outpatients—a cross-sectional hospital based survey in urban China," Health and Quality of Life Outcomes, vol. 8, article 62, 2010.
[17] J. J. vanNetten, P. E. Price, L. A. Lavery et al., "Prevention of foot ulcers in the at-risk patient with diabetes: a systematic review," Diabetes/Metabolism Research and Reviews, vol. 32, supplement 1, pp. 84–98, 2016.
[18] W.Clayton Jr. and T. A. Elasy, "A reviewof the pathophysiology, classification, and treatment of foot ulcers in diabetic patients," Clinical Diabetes, vol. 27, no. 2, pp. 52–58, 2009.
[19] V. Fejfarov´a, A. Jirkovsk´a, E. Dragomireck´a et al., "Does the diabetic foot have a significant impact on selected psychological or social characteristics of patients with diabetes mellitus?" Journal of Diabetes Research, vol. 2014, Article ID 371938, 7 pages, 2014.
[20] P. E. Norman, D. E. Schoen, J. M. Gurr, and M. L. Kolybaba, "High rates of amputation among Indigenous people inWestern Australia," Medical Journal of Australia, vol. 192, no. 7, p. 421, 2010.
[21] E. J. G. Peters and L.A. Lavery, "Effectiveness of the diabetic foot risk classification system of the international working group on the diabetic foot," Diabetes Care, vol. 24, no. 8, pp. 1442–1447, 2001.
[22] S. Morbach, H. Furchert, U. Gr¨oblinghoff et al., "Long-term prognosis of diabetic foot patients and their limbs: amputation and death over the course of a decade," Diabetes Care, vol. 35, no. 10, pp. 2021–2027, 2012.
[23] B. A. Lipsky, J. A. Weigelt, X. Sun, R. S. Johannes, K. G. Derby, and Y. P. Tabak, "Developing and validating a risk score for lower-extremity amputation in patients hospitalized for a diabetic foot infection," Diabetes Care, vol. 34, no. 8, pp. 1695– 1700, 2011.
[24] W. Amogne, A. Reja, and A. Amare, "Diabetic foot disease in Ethiopian patients: A Hospital Based Study," Ethiopian Journal of Health Development, vol. 25, no. 1, pp. 17–21, 2011.
[25] Z. G. Abbas, J. K. Lutale, and L. K. Archibald, "Diabetic foot ulcers and ethnicity in Tanzania: a contrast between African and Asian populations," International Wound Journal, vol. 6, no. 2, pp. 124–131, 2009.
[26] L. N.McEwen, K. R. Ylitalo, W. H. Herman, and J. S. Wrobel, "Prevalence and risk factors for diabetes-related foot complications in Translating Research into Action for Diabetes (TRIAD)," Journal of Diabetes and Its Complications, vol. 27, no. 6, pp. 588–592, 2013.
[27] D. G. Armstrong, K. Cohen, S. Courric, M. Bharara, and W. Marston, "Diabetic foot ulcers and vascular insufficiency: our population has changed, but our methods have not," Journal of Diabetes Science and Technology, vol. 5, no.6,pp. 1591–1595, 2011.
[28] L. Prompers, N. Schaper, J. Apelqvist et al., "Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease.The EURODIALE Study," Diabetologia, vol. 51, no. 5, pp. 747–755, 2008.
[29] S. H.Won, C. Y.Chung, M. S. Park et al., "Risk factors associated with amputation-free survival in patient with Diabetic foot ulcers," Yonsei Medical Journal, vol. 55, no. 5, pp. 1373–1378, 2014.
[30] S. Pscherer, F.-W. Dippel, S. Lauterbach, and K. Kostev, "Amputation rate and risk factors in type 2 patients with diabetic foot syndrome under real-life conditions inGermany," Primary Care Diabetes, vol. 6, no. 3, pp. 241–246, 2012.
[31] A. Korzon-Burakowska and P. Dziemidok, "Diabetic foot—the need for comprehensive multidisciplinary approach," Annals of Agricultural and EnvironmentalMedicine, vol. 18, no. 2, pp. 314– 317, 2011.
[32] M.-W. Sohn, R. M. Stuck, M. Pinzur, T. A. Lee, and E. Budiman-Mak, "Lower-extremity amputation risk after charcot arthropathy and diabetic foot ulcer," Diabetes Care, vol. 33, no. 1, pp. 98–100, 2010.
[33] D. K. Wukich, K. B. Hobizal, and M. M. Brooks, "Severity of diabetic foot infection and rate of limb salvage," Foot and Ankle International, vol. 34, no. 3, pp. 351–358, 2013.