THE PROFILE OF GERIATRIC EXTREMITY AMPUTATION IN A LOW-AND-MIDDLE-INCOME COUNTRY

U.E. Anyaehie, MBBS, FWACS, **O. Ede,** MBBS, FMC Ortho, FWACS, **G.O. Eyichukwu,** MBBS, FWACS, FICS, **G.O. Muoghalu,** MBBS, Dip Ortho (SiCOT), FWACS, FMC Ortho, **B.K. Emina,** MBBS, FMC Ortho, FWACS, Orthopaedic Department, Specialist Hospital, Asaba, Delta State, Nigeria, **W.I. Anetekhai,** MBBS, FMC Ortho, **S.O. Anigbamkpu,** MBBS, MWACS and **C.C. Nganwuchu,** MBBS, Plastic Department, National Orthopaedic Hospital, Enugu, Nigeria

Correspondence to: Dr. Solomon O. Anigbamkpu, Plastic Department, National Orthopaedic Hospital, Enugu, Nigeria. Email: solomonobiadi@gmail.com

ABSTRACT

Background: Despite advances in medical care and diagnosis, patients, particularly in low-and middle-income countries, continue to present with avoidable indications for amputation. Limb amputation is a substantial healthcare burden, especially in elderly individuals, as they tend to have comorbidities that either contribute to amputation or complicate their management.
Objective: This study aims to profile geriatrics that had extremity amputations and determine the causes and risk factors.
Methods: The study was a ten-year retrospective review of patients aged 65 years and above with amputation. Data were analyzed using SPSS version 26.
Results: A total of 124 patients were recruited. Males were 66(53.2%) and females were 58(46.8%). The mean age was 73.65 (SD=6.86) years. Diabetic foot disease was the leading cause of geriatric extremity amputations, occurring in 75 (60.48%) of the patients and the risk factors include poor glycaemic control, infections, peripheral neuropathy, and trivial traumas. Most patients presented late, with a median symptom duration of 30 days(maximum = 10950 and minimum = 1 day) before hospital presentation. Wagner grade 4(N=58)(46.77%) was the commonest grade of diabetic foot ulcer noted. About 80% of patients had one or more comorbidities, with hypertension and diabetes mellitus predominating. Microscopic proteinuria was recorded on urinalysis in 35(28.23%) patients, suggesting coexisting renal dysfunction. Twenty-nine patients (23.39%) had a significant surgical history, with previous limb amputation 13 (10.49%) being the most common surgical procedure. Below-knee amputation 72 (58.06%) was the commonest type in the study. Most patients (101 = 81.45%) had no complications following amputation, with 67(54.03%) discharged on a wheelchair.
Conclusions: This study found diabetic foot gangrene to be the leading cause of geriatric extremity amputations, with hypertension and diabetes mellitus the commonest comorbidities. It also found late presentation to be a common problem in these patients, with most patients presenting elsewhere first.

Key words: Geriatric, Extremity, Amputation, Low-and-middle-income countries, Comorbidities, Diabetes mellitus

INTRODUCTION

The ancient surgery of amputation remains a relevant lifesaving procedure in present times. Despite advances in medical care and diagnosis, patients, particularly in Low- and Middle-Income Countries (LMIC), still present with avoidable indications for amputation. This has become a healthcare burden, especially in the geriatric age group, as this group of patients tends to have comorbid problems that either result in or enhance the indication for amputation or complicate their management. Peripheral Artery Disease (PAD) appears to be the commonest indication for amputation among the elderly, with cardiopulmonary and metabolic risk factors present in the majority (1,2). This contrasts with general population reports of trauma being the commonest (3-5) and in some studies, diabetic foot gangrene was said to be the commonest indication (6,7) while still, some other studies find traditional bone setter gangrene top on their list (8,9). PAD is primarily seen in elderly patients with diabetes mellitus who often experience peripheral

neuropathy progressing to trophic ulcers and subsequent gangrene (10,11). Predominant risk factors for limb amputation may thus vary between societies and populations.

In the developed world, the major risk factor for extremity amputation is PAD among the geriatric age group which is contrary to diabetes is commoner in the LMIC (15). The poor health-seeking behaviour and the out-of-pocket payment in the LMIC is a major contributor to extremity amputation as the majority of the patients wound have tried various alternatives before presenting to tertiary institutions where specialized care can be offered (11,15).

The world's elderly population is on the increase (12) just as the lifetime risk for limb amputation has increased (13). The immediate post-operativee lower limb prosthetic application was found to reduce average rehabilitation time from 128 to 31 days in the USA as against the West African experience where the majority of the amputee never got a prosthetic replacement and they mobilize permanently on crutches which affect not only their social lives but also their economic activities in the society (12,15).

There is thus a need to see a healthier group as the consequences of amputation are enormous, ranging from psychological disturbances to general debilitation and functional impairment. There has been a marked improvement in limb preservation in high-income countries(14), but awareness and access to similar services may be lacking in low-income countries (6).

Studies on reasons for amputation will enhance education and knowledge on preventive measures. This study, therefore, seeks to profile elderly patients with limb amputations and identify the causes and risk factors, coexisting morbidity, and management.

MATERIALS AND METHODS

This was a retrospective review of amputations done in geriatric patients over ten years from January 2010 to December, 2019. Information retrieved from the folders includes socio-demographics, amputation indication, and level, diagnosis, Wagner grade for diabetic foot disease, risk factors for diabetic foot disease, time of hospital presentation and place of initial care, comorbidities, past surgical history, social history, haemoglobin levels at presentation, urinalysis findings, anaesthesia used, blood transfusions, perioperative complications, the outcome in terms of mortality and mobilization method at the point of discharge. Inclusion criteria were patients aged 65 years and above with amputation. Excluded were those with incomplete records. Ethical clearance was received for the study (IRB/HEC: S.313/IV/), and data were analyzed using SPSS version 26.

RESULTS

The records of 66 males (53.23%) and 58 females (46.77%) were studied. The mean age of the subjects was 73.65 years (SD = 6.86), with females slightly older than males at presentation (75.03 versus 72.52 years, respectively). Most patients were within the 65–74-year-old age group (Table 1). Many of the subjects were retired civil servants 37(29.84%) and farmers 28(22.58%). The rest were housewives 27(21.77%), traders 18(14.52%), artisans 5(4.03%), commercial drivers 2(1.61%), businessmen 2(1.61%), and others, constituting the remaining 5(4.05%).

Diabetic foot disease was the leading cause of geriatric extremity amputation in this study, accounting for 75(60.48%) of the cases (Table 2).

Table 1
The age categories of the patients

Age group (years)	No.	(%)
65-74	71	57.26
75-84	42	33.87
85-94	11	8.87
Grand Total	124	100.00

The lower limb was amputated in 122 (98.39%) patients, while the upper limb was only involved in 2(2.48%) patients. Eighty five subjects (68.55%) remembered no preceding trauma to the limb before symptom onset (Table3). Wagner grade 4(N=58, 46.77%) was the commonest grade of diabetic foot ulcer in patients with amputations for diabetic foot disease (Figure 1).

Table 2

The diagnosis of the study subjects

Diagnosis	No.	(%)
Diabetic foot gangrene	58	46.77
Vascular gangrene (PVD)	31	25.00
Diabetic foot ulcer	17	13.71
Marjolins ulcer/COM	4	3.23
Arterial ulcer	4	3.23
Traumatic amputation	2	1.61
Chronic leg ulcer	2	1.61
Malignant melanoma	1	0.81
Burn injury on upper limbs	1	0.81
Traumatic vascular gangrene	1	0.81
Infected TKR prosthesis	1	0.81
Failed ankle arthrodesis	1	0.81
Foot Kaposi's sarcoma	1	0.81
Grand Total	124	100.00

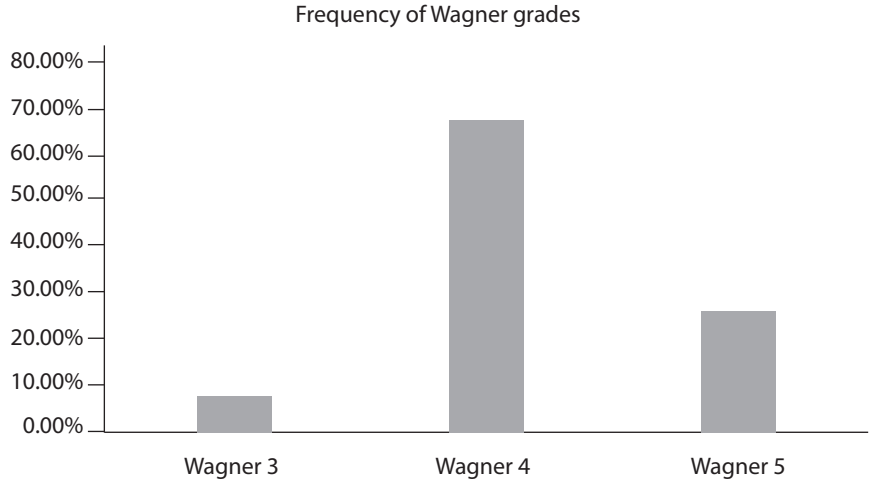
Table 3

History of preceding trauma to the limb

Preceding trauma to the affected limb	No.	(%)
None	85	68.55
Blunt foot injury	17	13.71
Penetrating foot injury	15	12.10
Rat bite	2	1.61
Snake bite	1	0.81
Insect bite, lymphedema	1	0.81
Burns	1	0.81
Machete cut	1	0.81
Post intervention, background PVD	1	0.81
Grand Total	124	100.00

Figure 1

The frequency of different Wagner grades in patients with diabetic foot disease



Most patients presented late to the National Orthopaedic Hospital Enugu (NOHE), with a median symptom duration of 30 days (maximum = 10950 and minimum = 1 day) before presentation at NOHE. When stratified by diagnosis, patients with chronic leg ulcers had the longest duration of symptoms (Table 4). Many patients sought initial care at private hospitals and traditional bone setters (TBS) before presenting to NOHE (Figure 2).

Table 4

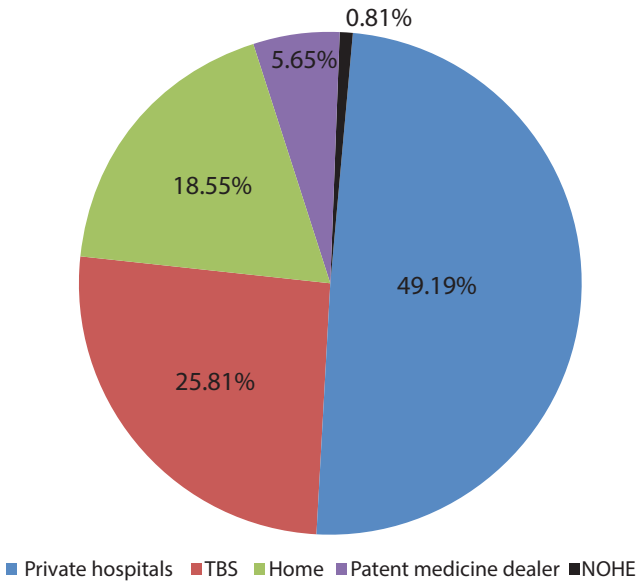
The median symptom duration before NOHE presentation

Diagnosis	Median symptom duration (days)	Max.*	Min.*
Chronic leg ulcer	5505	10950	60
Marjolins ulcer/COM	5475	8030	1825
Failed ankle arthrodesis	4015	-	-
Infected TKR prosthesis	2190	-	-
Malignant melanoma	1825	-	-
Arterial ulcer	198	1095	21
Diabetic foot ulcer	14	1825	7
Traumatic amputation	92	180	4
Foot Kaposi's sarcoma	90	-	-
Diabetic foot gangrene	30	1460	1
Vascular gangrene (PVD)	30	365	7
Burn injury upper limbs	7	-	-
Traumatic vascular gangrene	5	-	-

*Diagnoses that occurred once have no maximum or minimum, hence (-)

Figure 2

The place patients sought initial care for their symptoms



Only 26 (20.97%) of patients had no comorbidity, while the remaining had one or more comorbidities (Table 5), with hypertension 26(20.97%) and diabetes mellitus 31(25.00%) being the commonest conditions in this cohort. Although more than 50% of the patients have known comorbidities, only 22 (17.74%) were consistent with their medications. Twenty nine patients (23.39%) had a significant surgical history (Table 6), with a previous limb amputation being

the most common surgical procedure, with 13(10.49%) patients. Nineteen patients (15.32%) took alcohol and tobacco, 18 subjects (14.52%) took only alcohol, and two subjects (1.61%) took only tobacco.

Table 5

The frequencies of comorbidities seen in the patients

Comorbidities	No.	(%)
Hypertension and DM	32	25.81
DM	31	25.00
None	26	20.97
Hypertension	26	20.97
Hypertension and CVA	2	1.61
Hypertension CVA, and DM	2	1.61
DM and asthma	1	0.81
DM, glaucoma-induced blindness, breast cancer	1	0.81
Psychiatric disorder	1	0.81
Hypertension PUD, and DM	1	0.81
Hypertension and DM	1	0.81
Grand Total	124	100.00

Table 6

The past surgical history of the patients

Surgical history	No.	(%)
No previous surgery	95	76.61
Ray amputation	7	5.65
Herniorrhaphy	4	3.23
Below knee amputation	3	2.42
SSG leg venous ulcer	2	1.61
Cataract excision	2	1.61
Above knee amputation	2	1.61
Symes amputation	1	0.81
Glaucoma surgery	1	0.81
Prostate biopsy	1	0.81
Appendectomy	1	0.81
Ankle arthrodesis	1	0.81
ORIF distal tibiofibular fracture	1	0.81
TKR & diabetic foot ulcer debridement	1	0.81
Previous foot ulcer debridement	1	0.81
Mastectomy	1	0.81
Grand Total	124	100.00

The mean haemoglobin concentration of the patients was 9.95g/dl (SD = 2.61), with Kaposi's sarcoma 1(0.81%), traumatic vascular gangrene 1(0.81%), and diabetic foot gangrene 58(46.77%) presenting the lowest haemoglobin concentration. Thirty five patients (28.23%) had microscopic proteinuria on urinalysis, suggesting coexisting renal dysfunction. Of these 35 patients, 25 (71.43%) have diabetic foot disease.

Below-the-knee amputation (72 cases =58.06%) was the commonest amputation done in this study (Figure 3). Spinal anaesthesia was used in 112 cases (90.32%), general anaesthesia was used in 7(5.65%) patients, and a regional nerve block was used in

the remaining 5(4.03%) patients. Twenty three patients (18.55%) had significant postoperative complications, detailed in Table 7. Eighty two patients (66.13%) received an allogeneic blood transfusion during hospital admission, with 39.51% receiving one or two units of blood. One hundred and nineteen patients (95.97%) were discharged, while five (4.03%) died during hospital admission. Most patients 67(54.03%) were discharged on wheelchair mobilization, and the rest on Zimmer frame 48(38.71%) and axillary crutches 9(7.26%).

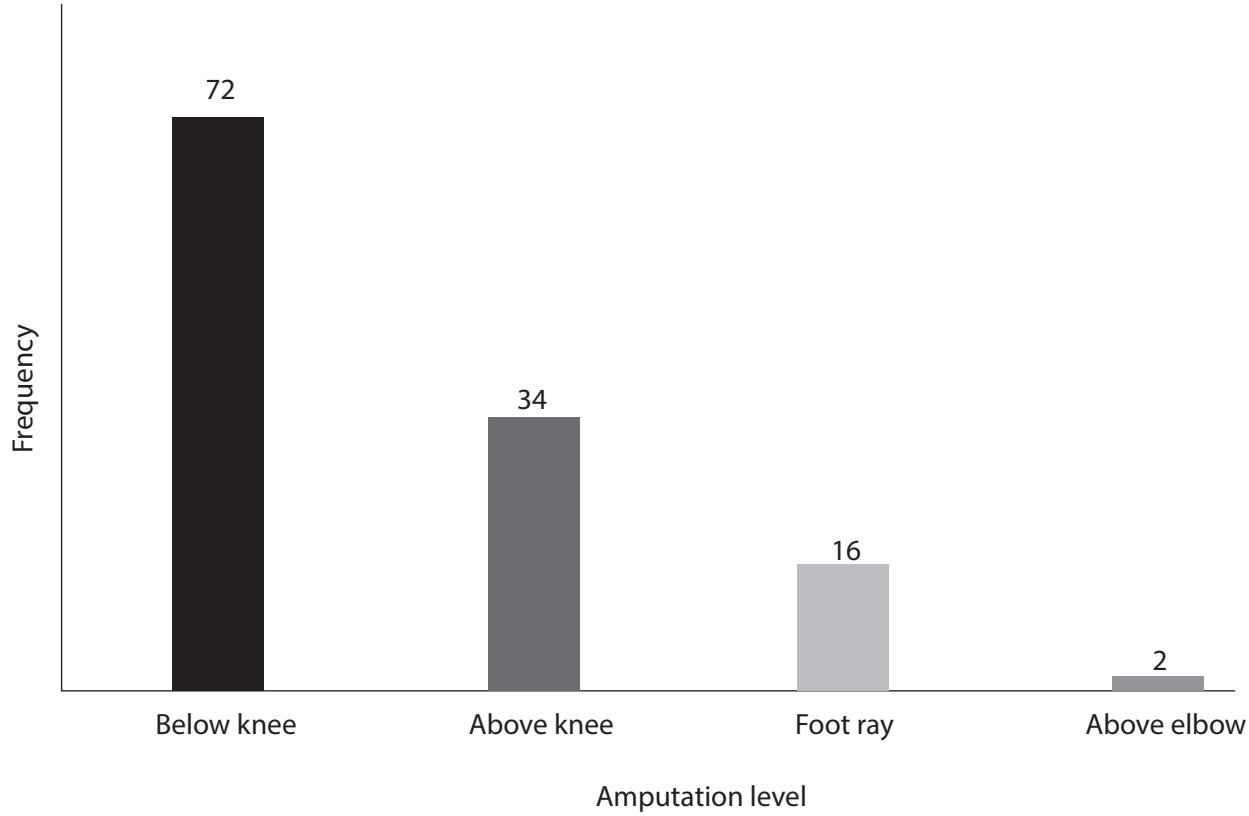
Table 7

Post-operative complications documented among the subjects

Post-operative complication	No.	(%)
None	101	81.45
Stump dieback	6	4.84
SSI	4	3.23
Death within 24 hours post-op.	3	2.42
CCF	2	1.61
Gluteal pressure sore	1	0.81
Depression, sacral pressure sore	1	0.81
Sacral pressure sore and psychosis	1	0.81
Wound breakdown	1	0.81
CVA	1	0.81
Persistent wound sinus	1	0.81
Psychotic breakdown	1	0.81
Ascending gangrene of the thigh (Hip disarticulation)	1	0.81
Grand Total	124	100.00

Figure 3

The amputation levels seen in the study



DISCUSSION

Amputation remains a common surgical operation in our environment where late presentation is common. Our study found more male patients than females receiving amputation,that concurred to other studies (6,8,15). The reason is likely because males are mostly involved in trauma (8) and, as breadwinners, resist the need to go to the hospital early until incapacitated. The majority of them were retired civil servants (29.84%), followed by farmers (22.58%). This proportion is in variance from a report by Salawu *et al.* (8) where the majority (46.8%) were farmers, most likely because the study was done in the northern region of Nigeria, where farming predominates. We found a decreasing frequency of extremity amputations with increasing age, probably because the life expectancy in our country is much lower at 55 years (16).

The mean age (73.65±6.86 years) is similar to the report by Greant and Van de Brande (1), who found the mean age of amputation to be 72 years.

Diabetes and peripheral arterial disease are the leading risk factors for lower limb amputations in our study, being in agreement to other studies (1,17,18). While diabetes alone was the leading aetiological factor in our study, in contrast to peripheral arterial disease which accounted for more limb amputations in other reports (17,18). In other studies done in Nigeria (6,7), diabetic foot gangrene was reported to be the major cause of limb amputation. Major amputations, which refer to amputations performed proximal to the ankle and wrist (5) were predominant in our study and compared similarly with other reports (6,8,15,18). This is likely because our patients do not present on time to hospital.

This study had Wagner grade 4 ulcers as the commonest presentation. This is in agreement to the findings by Ugwu *et al.* (19). This is probably because of late presentation with worsening of pathology, as the median symptom duration in our study was 30 (maximum = 10950 and minimum = 1) days. Patronage of TBS, patent medicine dealers, use of home therapies, and other hospitals were the predominant findings in our study. The likely reason is cost consideration, as health care in Nigeria is primarily out-of-pocket expenditure. These prevented the patients from getting a proper and early intervention for their limb pathology leading to gangrene and subsequent amputation. A painful and preventable factor, which was also reported by Nwosu *et al.* (4), where they noted a high amputation rate of 62.5% in children between 0-16 years in the aftermath of intervention by TBS.

No obvious trauma was noted in 85 (68.55%) of the patients in our study, but underlying multifactorial causes of diabetic foot ulcers have been described and include poor glycemic control, calluses, foot deformities, improper foot care, ill-fitting footwear, underlying peripheral neuropathy and poor circulation, dry skin, etc.(20).

This study showed that more than 50% of the patients had diabetes mellitus, which is not surprising, bearing in mind other studies that reported that patients with diabetes have a higher need for a major amputation up to five to ten times compared to non-diabetic patients with peripheral arterial disease (17,18). This is because of a combination of risk factors, including but not limited to vasculopathy, neuropathy, and infection. In addition, people with diabetes may exhibit non-compliance with medication, poverty, ignorance, and delay in seeking medical attention in LMICs. Poor compliance with medications noted in this study can be attributed to ignorance and poverty.

This study reported that 10.49% of the patients had previous limb amputations of different forms. This is worrisome as the risk of having a major limb amputation of the other limb after an ipsilateral major limb amputation has been reported to be high (21). So aggressive preventive measures are warranted once a person has an ipsilateral Lower Limb Amputation (LLA). These measures include timely management of skin and deep tissue infections/foot ulcers, optimization of regional blood supply, prevention of falls and stump injury, routine self-foot care, appropriate foot off-loading, and optimization of blood pressure, lipids, and glucose, and smoking cessation (22). Patient education is therefore imperative in geriatrics following limb amputation to reduce the incidence of subsequent contralateral limb amputation. Seventeen percent of these patients took tobacco, which has been reported as a risk factor that can be controlled to prevent complications leading to amputation (22) hence the need for adequate counselling on the need to stop tobacco use.

Also, anaemia was reported in most of our patients, which is a result of the chronicity of foot ulcers or gangrene. This trend has also been reported by Gezawa *et al.* (23), who noted a co-existing proteinuria in agreement with our study. We believe this is suggestive of coexisting renal dysfunction, which is not uncommon in diabetics, especially as most of the patients with proteinuria had diabetic foot disease.

Below-knee amputation was the commonest amputation done in our study, in agreement with some studies (7,8) but in contrast to the findings in others (4,6). This level of amputation was guided by a thorough clinical assessment with Doppler ultrasonography to determine the lowest and safest level of amputation that will allow for subsequent wound closure and prosthetic fitting.

Spinal anaesthesia was the commonest form of anaesthesia used for patients as it is considered safer in geriatric patients with comorbidities and a risk of perioperative complications. Nevertheless, some studies have reported that the mode of anaesthesia, whether regional or general, showed no difference in perioperative outcome following major lower limb amputations in functionally impaired geriatrics (24).

The commonest post-operative complications were issues with wound healing, similar to other studies where issues with wound and wound infection were the commonest post-operative complication (6,8). This is likely because of the comorbidities present, impairing wound healing.

Most patients in our study received blood transfusions due to anaemia, which is expected for the wound to heal and early recovery. Similar findings were reported by Gezawa *et al.* (23), who also noted that anaemia was significantly associated with poor wound healing, amputation, and mortality.

The majority of our patients were discharged home while 5 (4.03%) died during admission, in contrast to a study that reported death within 30 days in more than 11% of patients who underwent major amputation (25). This is because their study was on patients with diabetes, not a mixed cohort as in this study.

Patients discharged in a wheelchair were more than those discharged with a walking aid, which could be from several factors ranging from functional impairment, age, and comorbidities topsychological issues with amputation. A study by Melsom and Danjoux (26) advised that once done with immediate post-operative care, there should be a prompt referral to a local amputee rehabilitation team for early mobilization and physiotherapy to prevent cardiovascular and peripheral vascular diseases. Other studies have reported functional affectation after amputation with general deconditioning and loss of mobility, especially if the onset of rehabilitation is delayed and there is a lack of social support upon return to the community (27). Therefore, early physiotherapy with mobilization, psychotherapy, and social support are needed for geriatric amputees.

CONCLUSION

Diabetic foot gangrene is the commonest cause of major lower limb amputation in our study, with chronic leg ulcers and diabetes as the dominant risk factors for developing gangrene. Previous limb amputation is a risk factor for having a major lower limb amputation. Early presentation to hospitals capable of handling chronic leg ulcers, particularly in diabetics, is needed.

REFERENCES

1. Greant, P. and Van den Brande P. Amputation in elderly and high-risk vascular patients. *Annals Vasc Surg*. 1990; **4**(3): 288-290.
2. Abou-Zamzam, A.M., Ternya, T.H. and Killeen, J.D. Major lower extremity amputation in an academic vascular centre. *Ann Vasc Surg.* 2003; **17**: 86-90.
3. Omoke, N.I., Chukwu, C.O., Madubueze, C.C., and Egwu, A.N. Traumatic extremity amputations in a Nigerian setting: patterns and challenges of care. *Int Orthop.* 2010; **36**:613-618.
4. Nwosu, C., Babalola, M.O., Ibrahim, M.H. and Suleiman, S.I. Major limb amputations in a tertiary hospital in North Western Nigeria. *Afr Health Sci.* 2017; **17**: 508-512doi: 10.4314/ahs.v17i2.26. PMID: 29062347; PMCID: PMC5637037.
5. Ajibade, A., Akinniyi, O.T. and Okoye, C.S. Indications and complications of major limb amputations in Kano Nigeria. *Ghana Med J.* 2013; **47**:185-188.
6. Onyemaechi, N.O.C., Oche, I.J., Popoola, S.O., Ahaotu, F.N. and Elachi, I.C. Aetiological factors in limb amputation: The changing pattern! *Nigerian J Orthop Trauma.* 2012; **11**(2): 63-67
7. Dada, A.A. and Awoyomi, B.O. Is the trend of amputations in Nigeria changing? A review of 51 consecutive cases seen at Federal Medical Centre EbutteMetta Nigeria. *Niger J Med.* 2010; **15**:167-169.
8. Salawu, O.N., Babalola, O.M., Mejabi, J.O., Fadimu, A.A., Ahmed, B.A., Ibraheem, G.H., *et al.* Major extremity amputations: Indications and post surgery challenges in a Nigeria tertiary institution. *Sahel Med J.* 2019; **22**: 8-12.
9. Akinyoola, A.L., Oginni, L.M., Adegbehingbe, O.O., Orimolade, E.A. and Ogundele, O.J. Causes of limb amputation in Nigerian children. *West Afr J Med.* 2006; **25**:273-275.

10. Gabel, J., Jabo, B., Patel, S., Kiang, S., Bianchi, C., Chiriano, J., *et al*. Analysis of patients undergoing major lower extremity amputation in the vascular quality initiative. *Ann Vasc Surg*. 2018; **46**:75-82.
11. Lipsky, B.A., Berendt, A.R., Deery, H.G., Embil, J.M., Joseph, W.S., Karchmer, A.W., *et al*. Diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2004; **39**(7):885-910.
12. United Nations, Department of Economics and Social Affairs, Population Division(2019). World Population Ageing 2019: Highlights.
13. Beverly, T., Rodrigues, Venkat, N.,Usman V. andMalabu, H. Prevelence and risk factors for diabetic lower limb amputation: a clinic based case study. *J Diabetes Res*. 2016, ID 5941957; **1**-7.
14. Khan, T., Shin, L., Woelfel, S. and Rowe, V. Building a scalable diabetic limb preservation program: Four steps to success. *Diabetic Foot and Ankle*. 2018; **9**(11): 1-4.
15. Obalum, D.C. and Okeke, G.C. Lower limb amputations at a Nigerian private tertiary hospital. *West Afr J Med*. 2009; **28**(1):24-27.
16. Data.worldbank.org. Life expectancy at birth, total (years)-Nigeria. Available at: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=NG. (Accessed:10/07/2022).
17. Carmona, G.A, Hoffmeyer, P., Herrmann, F.R., Vaucher, J.,Tschopp, O., Lacraz, A. and Vischer, U.M. Major lower limb amputations in the elderly observed over ten years: the role of diabetes and peripheral arterial disease. *Diabetes Metab*. 2005; **31**(5):449-454.
18. Kristensen, M.T. Holm, G.and Gebuhr, P. Very low survival rates after non traumatic lower limb amputation in a consecutive series. *Interactive Cardiovasc Thoracic Surg*. 2012; **14**(5):543-547.
19. Ugwu, E., Adeleye, O., Gezawa, I., Okpe, I., Enamino, M. and Ezeani, I. Burden of diabetic foot ulcer in Nigeria: Current evidence from the multicenter evaluation of diabetic foot ulcer in Nigeria. *World J Diabetes*. 2019; **10**(3):200-211.
20. Oliver, T.I. and Mutluoglu, M. Diabetic foot ulcer. [Updated 2022 Aug 8]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537328/
21. Johannesson, A., Larsson, G.U., Ramstrand, N., Turkiewicz, A., Wirehn, A.B. and Atroshi, I. Incidence of lower-limb amputation in the diabetic and nondiabetic general population: a 10-year population-based cohort study of initial unilateral and contralateral amputation and reamputations. *Diabetes Care*. 2009; **32** (2):275-280.
22. Huseynova, K., Sutradhar, R., Booth, G.L., Huang, A. and Ray, J.G. Risk of contralateral lower limb amputation and death after initial lower limb amputation - a population-based study. *Heliyon*. 2018; **4**(10):e00836. doi: 10.1016/j.heliyon.2018.e00836. PMID: 30320234; PMCID: PMC6180416.
23. Gezawa, I.D., Ugwu, E.T., Ezeani, I., Adeleye, O., Okpe, I. and Enamino, M. Anemia in patients with diabetic foot ulcer and its impact on disease outcome among Nigerians: Results from the MEDFUN study. *PLoS One*. 2019 **17**;14(12):e0226226. doi: 10.1371/journal.pone.0226226. PMID: 31846473; PMCID: PMC6917259.
24. Moreira, C.C., Alik Farber, A., Kalish, J.A., Eslami, M.H., Didato, S., Rybin, D., Doros, G. and Siracuse, J.J. The effect of anesthesia type on major lower extremity amputation in functionally impaired elderly patients. *J Vascular Surg*. 2016; **63** (Issue 3}:696-701.
25. Gurney, J.K., Stanley, J., Rumball-Smith, J., York, S. and Sarfati, D. Post-operative death after lower-limb amputation in a national prevalent cohort of patients with diabetes. *Diabetes Care*. 2018; **41**(6):1204–1211. https://doi.org/10.2337/dc17-2557.
26. Melsom, H. and Danjoux, G. Perioperative care for lower limb amputation in vascular disease. *Continuing Education in Anaesthesia Critical Care Pain*. 2011; **11** (5): 162–166.https://doi.org/10.1093/bjaceaccp/mkr024
27. Frieden, R.A. The geriatric amputee. *Phys Med Rehabil Clin N Am*. 2005; **16**(1): 179-195. Doi:10.1016/j.pmr.2004.06.004. PMID: 15561550.