

# Amputation-Related Phantom Limb Pain in Nigeria: A Prospective Cohort Study

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## Abstract

**Background:** Phantom limb pain (PLP) is a common and distressing complication of limb amputations. Literature on PLP in Nigeria and indeed Africa is scant despite the high rate of amputations in published works. We sought to highlight the burden of PLP among Nigerian amputees in order to improve awareness and care by health-care providers. **Patients and Methods:** In this prospective cohort study, consecutive limb amputees were recruited and relevant data were collected by in-person interview at 1 week postamputation and subsequently by telephone survey at 6 months and 12 months. The sociodemographic and clinical information of the amputees were recorded, as well as presence of PLP and the treatment offered by the attending physician. The Chi-square test of statistical significance and multivariate analysis using binary logistic regression were used in the analysis, and the level of statistical significance was determined by  $P < 0.05$ . **Results:** One hundred and fourteen consecutive limb amputations were carried out in 113 patients over a 1-year period. The period prevalence of PLP was 63.6%, and of these, only 8.6% had this documented in their medical record. No predictor of PLP was identified in the cohort. **Conclusion:** PLP is highly prevalent among limb amputees in our cohort. We call for improved awareness and practice relating to PLP among health-care providers and partners, considering the vast population of amputees in the region.

**Keywords:** Africa, American Society of Anesthesiologists physical status grade, amputees, phantom limb pain

## INTRODUCTION

Pain is an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage. Phantom limb pains (PLPs) are painful sensations referred to absent limbs. With the foregoing in mind, PLP must be differentiated from entities such as “phantom limb sensation (PLS)” and “stump pain/residual limb pain (RLP).” PLP phenomenon was first described in 1552 by the French surgeon, Ambroise Pare, but the title was given to this entity in 1872 by the American neurologist, Silas Weir Mitchell. PLP is a real pain and can range from brief flashes of mild pain to constant severe pain. It is a common complication of limb amputations with a reported prevalence of 72% in a study.<sup>[1]</sup> Whereas most PLPs arise from amputated limbs, congenital limb absence accounts for a lesser prevalence.<sup>[2]</sup>

## Limb amputations in Nigeria

Limb amputations are common orthopedic surgical procedures in Nigeria and provide a major means of saving lives when

limb salvage is not feasible, especially with patients presenting late to health-care facilities with advanced limb pathologies. A national review of extremity amputations in Nigeria using data collected over two decades ago had reported the following indications for amputation; trauma (34%), complication following traditional bone setting (23%), malignant tumors (14.5%), diabetic gangrene (12.3%), infections (5.1%), peripheral artery disease (2.1%), and burns (2.1%).<sup>[3]</sup> Recent data, however, indicate a changing trend with a greater preponderance of diabetic foot gangrene as the most common indication for limb amputations<sup>[4-6]</sup> or following closely after trauma and gangrene from traditional bonesetters mismanaged fractures.<sup>[7,8]</sup> This is not unexpected

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given the predicted global increase in the prevalence of diabetes from 2011 to 2030 estimated at 50.7%, with an average annual growth of 2.7%, which is 1.7 times the annual growth of the total world adult population.<sup>[9]</sup>

### Phantom limb pain in Nigeria

In contrast to the known high prevalence of PLP among amputees worldwide, it is an understatement to say that this common distressing complication of amputation is underrecognized, unreported, or simply ignored by health-care workers here in Nigeria. Studies of PLP in Nigeria and indeed Africa are sparse or nonexistent. A literature search did not find any previous study of PLP in Nigeria, but we found three studies on complications of limb amputation remotely mentioning PLP with a very low prevalence of 5.5%, 3.3%, and 14.6%, respectively.<sup>[5,7,10]</sup>

### The phantom limb pain challenge

PLP is a chronic neuropathic pain that adversely affects patients' quality of life, and amputees with phantom pain have been found to have a poorer health-related quality of life than amputees without phantom pain.<sup>[11]</sup> The morbidity associated with PLP is considerable, with some patients having severe pain intensity, limitation of social activities, depression, loss of sleep, and attempted suicides.<sup>[12]</sup> The plight of the amputees with PLP is worsened because the mechanisms underlying PLP are so poorly understood that 33% of the PLP patients report that their health-care providers told them there was no treatment available.<sup>[13]</sup> Several treatment options ranging from pharmacological to physical and surgical interventions have been offered to the patients suffering from PLP, yet a good proportion reports no relief or clinical improvement in spite of all these offerings.<sup>[14]</sup> With the increasing incidence of limb loss in Nigeria and elsewhere,<sup>[15,16]</sup> there is growing interest in preventing or treating PLP. This highlight on the underrecognition and undertreatment of PLP among Nigerian amputees is intended to provide the impetus for improved awareness and care by health-care providers in Africa.

### Methodology

#### Ethical consideration

Ethical approval for the study with protocol number: 201 was obtained from the Institutional Review Board of National Orthopaedic Hospital, Enugu. The respondents were required to sign to a written informed consent form, and for children, this was obtained from their parents or guardians. Participation in the study was voluntary, with respondents being absolutely free to withdraw at any stage as they may wish. The respondents were assured that information obtained from them would be treated anonymously and confidentially.

#### Setting

This is a prospective cohort study conducted in National Orthopedic Hospital, Enugu, a tertiary regional trauma center in Nigeria involving sequential limb amputees recruited over a period of 1 year which commenced on April 1, 2015.

### PATIENTS AND METHODS

Informed consent was sought from all patients who underwent limb amputation; major or minor and all consenting amputees were consecutively enrolled in the study. For children and minors, the informed consent was obtained from their parents or guardians.

#### Exclusion criteria

Amputees were excluded if their hospital stay after admission was for a period of <7 days; on account of discharge, death or transfer to another facility. All amputees who did not give consent to participate in the study or who had a history of dementia were also excluded.

#### Data collection

Information sought in the pro forma for data collection included the demographic data of the patient (such as gender, age, occupation, educational level, and contact telephone), American Society of Anesthesiologists (ASA) physical status grade, any existing comorbidity, technique of anesthesia used for the amputation, cause of the pathology indicating the amputation, site of extremity of the surgery, level of amputation, any documented recognition of PLP in the patient's medical record by the managing health-care providers, and any treatment offered for the PLP. Patients were assessed postoperatively in hospital at 1 week, at 6 months, and 12 months by telephone for the presence of PLP, including the description of the pain from a list of words provided and its intensity. Detailed explanation was given to the amputees in order to distinguish PLP from other components of the phantom limb phenomena such as residual limb/stump pain and nonpainful phantom sensation. The 11-point Numeric Rating Scale (NRS) was used to assess pain intensity as 0 for no pain and 10 for worst imaginable pain. For level of amputation, major amputation was defined as amputations proximal to or through the ankle in the lower limb or the wrist in the upper limb, whereas minor amputation was defined as preservation of at least part of the foot or hand.

After discharge from the hospital, all the participants were evaluated by telephone survey at 6 months and 12 months for the presence of PLP, including a description of the pain and its intensity, in continuation of the direct face-to-face assessment done while on admission at 1 week postamputation.

At 2 years from the commencement of the study, when the last recruited participant had been surveyed for the presence of PLP, the medical records of all the participants with PLP were reviewed, and any documentation, comment, or treatment regarding PLP by any health-care worker (surgeons and physiotherapists) was noted.

#### Statistical analysis

Data entry and statistical analysis was performed using IBM Statistical Package for the Social Sciences SPSS (version 22, SPSS Inc., Chicago, Illinois, USA) for Windows. Frequency distributions and cross-tabulations were generated. The Chi-square test of statistical significance and multivariate

analysis using binary logistic regression were used in the analysis, and the level of statistical significance was determined by  $P < 0.05$ .

In determining the factors affecting PLP, the age of the respondents was categorized into three groupings including those <40 years, 40–64 years, and those 65 years and above.

Variables that had  $P < 0.2$  on bivariate analysis (including age of respondents in groups, presence of comorbidities, ASA grade of respondent, and diagnosis before amputation) were entered into the logistic regression model to determine the predictor of PLP. The result of the logistic regression analysis is reported using adjusted odds ratio and 95% confidential interval, and the level of statistical significance was determined by  $P < 0.05$ .

## RESULTS

One hundred and fourteen limb amputations were carried out in 113 patients over the period of 1 year, with one patient being admitted twice during the course of the study for the amputation of the second lower limb on the same account due to diabetic foot gangrene. Six of the amputees died during the 1-year period of follow-up, and as such, their PLP status could not be fully ascertained. Of these, three died within 3 days postoperative of septicemia associated with diabetic foot gangrene and neglected traumatic wounds, whereas the other three died later within 6 months of the surgery from unknown causes outside the period of hospital admission. All the patients approached for informed consent agreed to take part in the cohort study, and the only dropouts were those indicated above. The amputees including those who had minor limb amputations stayed on admission in our health facility for a minimum duration of 1 week in consideration of the safety of the prevailing environment in their respective homes, the risk of nosocomial infections in the hospital notwithstanding.

Table 1 shows the sociodemographic and clinical characteristics of the amputees. The mean age of the respondents was 49.5 (20.5) years, with a minimum age of 9 years and maximum of 103 years. Majority of the amputations were in males, 76/114 (66.7%), whereas most of the amputations were carried out in the lower limb, 106/114 (93%). Major amputations were predominant, 107/114 (93.7%). Diabetic foot gangrene was the leading indication for amputation, 43/114 (37.7%), and this was closely followed by trauma, 38/114 (33.3%). Among the six patients who had amputation on account of miscellaneous causes, five resulted from chronic osteomyelitis, whereas one had lymphedema praecox. Based on the level of the amputations, only 6.1% (7/114) were minor. The majority of the amputees were ASA Grade III at the time of amputation, 52/114 (45.6%), and regional anesthesia was the predominant anesthetic technique used, 100/114 (87.7%). The three patients that died before the first observation at 1 week had no opportunity of reporting PLP; as such, only the 110 who were interviewed at 1 week were considered in determining the prevalence of PLP in the cohort.

**Table 1: Sociodemographic and clinical characteristics of the amputees (n=114)**

Variable	Frequency (%)
Age (years)	
Mean±SD	49.5 (20.5)
Minimum	9.0
Maximum	103
Age of respondents in groups (years)	
9-39	36 (31.5)
40-64	46 (40.4)
≥65	32 (28.1)
Gender	
Male	76 (66.7)
Female	38 (33.3)
Anesthesia technique	
General	14 (12.3)
Regional	100 (87.7)
Site of amputation	
Upper limb	8 (7.0)
Lower limb	106 (93.0)
Level of amputation	
Major	107 (93.9)
Minor	7 (6.1)
Presence of comorbidities	
Yes	71 (62.3)
No	43 (37.3)
Educational attainment of respondents	
No formal education	8 (7.0)
Primary education	37 (32.5)
Secondary education	44 (38.6)
Postsecondary education	25 (21.9)
Occupation	
Civil/public servant	20 (17.5)
Trading	38 (33.3)
Farming	12 (10.5)
Artisan	25 (21.9)
Unemployed	6 (5.3)
Schooling	13 (11.4)
ASA physical status grade	
Grade I	20 (17.5)
Grade II	36 (31.6)
Grade III	52 (45.6)
Grade IV	6 (5.3)
Diagnosis before amputation	
Diabetic foot gangrene	43 (37.7)
Trauma	38 (33.3)
Miscellaneous (Infection, etc.)	6 (5.3)
Malignancy	12 (10.5)
Vascular gangrene	15 (13.2)

ASA – American Society of Anesthesiologists physical status grade, SD – Standard deviation

The period prevalence of PLP during the 1-year follow-up postamputation was 63.6% (70/110). The patient who had amputation of both lower limbs reported PLP in one limb but not in the other. Only 8.6% (6/70) of the participants reporting PLP had a documentation of PLP status in their case file

by caregivers, and of these, three were treated with simple analgesics and/or adjuvants, two received counseling and reassurance, whereas one was just ignored [Table 2].

Tables 3 and 4 indicate that the predominant character of PLP among the amputees was described as the “biting” and “aching” types. Majority of the PLP sufferers experienced pain of mild (NRS: 1–3) or moderate intensity (NRS: 4–6), with only two patients reporting severe pain: one 7/10 and the other 8/10 on the NRS, and these were within the 1<sup>st</sup> week postamputation. Of the 70 amputees who reported PLP (not shown in the tables) 39 (55.7%) reported their highest pain score was in the mild pain range, 29 (41.4%) reported their highest pain score to be in the moderate range, and two (2.9%) reported the highest pain score to be severe. Of the 70 amputees who experienced PLP, most had early onset of PLP, with 97% (68/70) developing it within 1 week following amputation. At 6-month follow-up, 30 amputees were experiencing PLP, whereas at 12-month follow-up, only 9 amputees were experiencing PLP. The character of the pain and its intensity also varied over time, with most patients having decreasing pain intensity. Three of the amputees in this study (4.3%), however, reported progressively worsening PLP even at 1 year after amputation.

None of the sociodemographic and clinical factors were found to be associated with the development of PLP. The ASA grade of the amputees at amputation which yielded a *P* value of 0.019 on bivariate analysis when subjected to binary logistic regression analysis was not significant, implying that it was a confounding factor [Table 5].

## DISCUSSION

The results of the present study indicate that PLP is a very common complication of limb amputations but poorly recognized and undertreated. The sheer magnitude of limb amputations in this single-center study over a period of 1 year provides a stimulus to investigate this population of patients for a common complication associated with amputations, namely PLP. With a limb amputation rate of 114/year in this center, the figure is far greater than that of some other tertiary health-care institutions reported in Nigeria: 94/10 years,<sup>[4]</sup> 90/2 years,<sup>[5]</sup> 165/7 years,<sup>[6]</sup> and 192/11 years,<sup>[7]</sup> respectively.

### Prevalence of phantom limb pain

The period prevalence of PLP (63.6%) obtained in the present study during the 1-year follow-up is in contrast to the very low prevalence of 5.5%,<sup>[5]</sup> 3.3%,<sup>[7]</sup> and 14.6%<sup>[10]</sup> quoted in three Nigerian sources which remotely mentioned PLP while considering complications of limb amputation. The data on PLP in these three quoted studies with very low prevalence of PLP were extracted retrospectively from caregiver documentation in the patient’s case files. This method of data collection with regard to PLP has been known to grossly underestimate its prevalence since most of the patients do not spontaneously volunteer information about experiencing PLP for fear of being stigmatized as having spiritual or psychiatric problems to the extent of complaining of pain in absent limb.

**Table 2: Phantom limb pain outcome (n=110)**

Variable	Frequency (%)
Presence of PLP	
Yes	70 (63.6)
No	40 (36.4)
PLP documented in case file	
Yes	6 (8.6)
No	64 (91.4)
Any treatment given for PLP	n=6
Yes	5 (83.3)
No	1 (16.7)
Type of treatment given	
Counseling/reassurance	2 (40.0)
Carbamazepine tablets	1 (20.0)
Chlorzoxazone/diclofenac/paracetamol tablets	1 (20.0)
Pregabalin/diclofenac tablets	1 (20.0)
PLP – Phantom limb pain	

**Table 3: Descriptors of the phantom limb pain among the amputees over time (n=70)**

Variable	Frequency (%)
Type of pain (1 week)	
Burning	2 (2.9)
Biting	44 (62.9)
Throbbing	3 (4.3)
Aching	12 (17.1)
Itching	4 (5.7)
Pricking	3 (4.3)
Nil	2 (2.9)
Type of pain (6 months)	
Burning	2 (2.9)
Biting	9 (12.9)
Throbbing	5 (7.1)
Aching	11 (15.7)
Itching	1 (1.4)
Pricking	2 (2.9)
Nil	40 (57.1)
Type of pain (1 year)	
Burning	3 (4.3)
Biting	4 (5.7)
Pricking	2 (2.9)
Nil	61 (87.1)

This underrecognition of PLP prevalence by data acquired from this source was also underscored by a retrospective survey which revealed that only 40% of those who admitted having PLP had it documented in their medical record by health-care providers (doctors, nurses, and physical therapists) despite the long months/years since amputation.<sup>[17]</sup> If the data in the present study had been sourced from the amputees’ case files, only 6 out of 110 participants would have been identified as developing PLP, resulting in a prevalence of 5.5% being quoted, clearly an underestimate of the prevalence obtained upon explicitly asking patients about their PLP experience.

**Table 4: Intensity of phantom limb pain among the amputees over time (n=70)**

Variable	Frequency (%)
Pain intensity-NRS (1 week)	
One	1 (1.4)
Two	18 (25.7)
Three	20 (28.6)
Four	12 (17.1)
Five	9 (12.9)
Six	6 (8.6)
Seven	1 (1.4)
Eight	1 (1.4)
Nil	2 (2.9)
Pain intensity-NRS (6months)	
One	9 (12.9)
Two	18 (25.7)
Three	1 (1.4)
Four	1 (1.4)
Five	1 (1.4)
Nil	40 (57.1)
Pain intensity-NRS (1 year)	
One	4 (5.7)
Two	2 (2.9)
Four	1 (1.4)
Five	1 (1.4)
Six	1 (1.4)
Nil	61 (87.1)

NRS – Numeric Rating Scale pain score

Jensen *et al.* had found a PLP incidence of 72%, 65%, and 59%, respectively, at 8 days, 6 months, and 2 years after limb amputation in a prospective study involving 58 patients.<sup>[18]</sup> Another prospective study, multicenter, by Bosmans *et al.* on 85 limb amputees reported PLP prevalence rates of 32%, 27%, 23%, and 27% from the 73 lower-limb amputees and 50%, 78%, 57%, and 67% from the 12 upper limb amputees at 6 months, 1½ years, 2½ years, and 3½ years, respectively.<sup>[19]</sup> In the latter study, however, only PLP sufferers who experienced it a few times a day or more frequently were recognized, whereas those who experienced it a few times a week or less frequently were excluded. This introduction of cutoff point for recognition of existing PLP probably explains the low prevalence in their study. Furthermore, 6 months after amputation when the first observation of PLP was due, 37% of the initially recruited 134 amputees had been lost to follow-up because they died or dropped out. Thus, out of the initial amputee population of 225, 134 were eventually recruited, and of these, 37% were lost to follow-up because they died or dropped out within the first 6 months when the first observation for PLP was due, leaving only 85 (37.8% of the amputee population) for consideration and analysis. This number further declined to 18 by the time of the fourth observation at 3½ years postamputation for sundry reasons. How these losses would impact the representative nature of their amputee population is a matter of conjecture. Further insight into the impact of methodology on the prevalence rate quoted for PLP in different studies is provided

by the Wartan *et al.* study which was a retrospective survey in a very elderly population of all male, traumatic amputees, in which 87% of the respondents had a lost limb 30–50 years earlier.<sup>[13]</sup> Out of 590 amputees initially recruited for the study, only 508 eventually provided categorical responses on PLP presence or otherwise, and of these, 326 affirmed experiencing PLP. The authors quoted a prevalence of 55.2% (326/590) in what ought to be 64.2% (326/508).

Another potential source of the wide difference in PLP prevalence quoted in some studies is the difficulty which the respondents may have in discriminating between PLP, PLS, and RLP.<sup>[20]</sup> In the study by Wartan *et al.*, 18 out of 526 respondents categorically declared this confusion<sup>[13]</sup> and a much higher number may be silent about their confusion or may not know that they are making false declaration. It was in recognition of this potential pitfall that this study ensured that the first assessment was done as a face-to-face interview, with detailed explanation to enable the amputees discriminate PLP, from PLS and RLP. Although undocumented as part of the data in this study, in the course of this direct interview, most of the PLP sufferers expressed surprise and some relief that someone knows and cares about their otherwise silent and embarrassing agony which they were scared to report for fear of social recrimination in respect of “complaint of pain in nonexistent limb.”

The only study to date conducted in Africa on PLP was about two decades ago in the year 2000 by Lacoux *et al.* which reported a low prevalence of PLP: 32.5% (13/40) of the amputees and 29% (15/51) of the amputations.<sup>[21]</sup> Their work was a cross-sectional survey of traumatic upper limb amputees conducted in Amputee Camp in Sierra Leone. The fact that their study was limited to traumatic upper limb amputees (also with exclusion of amputations distal to the wrist) and meant as an initial assessment of 40 out of 153 upper limb amputees in the camp without any random sampling being applied may all have affected the representative nature of their cohort with respect to PLP. The authors further disclosed communication challenges with the amputees who predominantly spoke the local Krio language and that translations into Krio were not exact or not available, despite using interpreters. There was also a tense and deteriorating security situation during the pain assessment which forced the researchers to hurriedly and prematurely conclude the study and evacuate; both constraints which they acknowledged could account for the low prevalence of PLP in their study. It was also revealed that during the surgical amputation procedures, all the patients in the Lacoux *et al.* study<sup>[21]</sup> had been anesthetized with ketamine, a N-methyl-D-aspartate receptor antagonist with reports of efficacy in the treatment of some neuropathic pains,<sup>[22,23]</sup> but any contribution by this to the low prevalence of PLP in their study cannot be presumed. However, these logistical and methodological issues may have contributed to the low prevalence of PLP in their study.

Prevalence studies on PLP also contend with the fact that many amputees have had multiple amputations, and as such, while

**Table 5: Prevalence of phantom limb pain and associated factors in the amputees**

Variable	Phantom limb pain (n=111)		P*	AOR (95%CI) <sup>§</sup>
	Yes, n (%)	No, n (%)		
Age of the amputees in groups (years)				
<40	27 (75.0)	9 (25.0)	0.193	0.8 (0.2-4.5)
40-64	25 (58.1)	18 (41.9)		0.5 (0.1-1.8)
≥65	18 (56.2)	14 (43.8)		1
Gender				
Male	45 (61.6)	28 (38.4)	0.668	NA
Female	25 (65.8)	13 (34.2)		
Anesthesia technique				
General	9 (64.3)	5 (35.7)	0.919	NA
Regional	61 (62.9)	36 (37.1)		
Site of amputation				
Upper limb	5 (62.5)	3 (37.5)	0.973	NA
Lower limb	65 (63.1)	38 (36.9)		
Degree of amputation				
Major	65 (62.5)	39 (37.5)	0.636	NA
Minor	5 (71.4)	2 (28.6)		
Presence of comorbidities				
Yes	39 (56.5)	30 (43.5)	0.067	1.6 (0.2-15.3)
No	31 (73.8)	11 (26.2)		1
ASA grade of the amputees				
Grade I	11 (55.0)	9 (45.0)	0.019	1.0 (0.04-24.7)
Grade II	30 (83.3)	6 (16.7)		7.3 (0.4-131.0)
Grade III	28 (53.8)	24 (46.2)		1.7 (0.1-22.1)
Grade IV	1 (33.3)	2 (66.7)		1
Diagnosis before amputation				
Diabetic foot gangrene	20 (48.8)	21 (51.2)	0.139	0.7 (0.2-2.6)
Trauma	28 (75.7)	9 (24.3)		2.8 (0.2-33.3)
Miscellaneous (Infection, etc.)	4 (66.7)	2 (33.3)		4.6 (0.3-81.2)
Malignancy	9 (75.0)	3 (25.0)		1.9 (0.2-17.1)
Vascular gangrene	9 (60.0)	6 (40.0)		1

\*P value on bivariate analysis, §AOR (95% CI) on multivariate analysis. ASA – American Society of Anesthesiologists physical status grade, NA – Not applicable, AOR – Adjusted odds ratio, CI – Confidence interval

some authors have used the total number of amputees as the reference population sample, others opted for the total number of amputations in their computation of PLP prevalence, as shown in the study by Lacoux *et al.* reporting a prevalence of PLP: 32.5% (13/40) of the amputees and 29% (15/51) of the amputations;<sup>[21]</sup> thus, interpretation of the prevalence quoted in PLP studies should be made with circumspection. This does not appear to have been an issue in the present study as only one participant had two amputations; the rest had one.

### Phantom limb pain characteristics

The onset of PLP among the amputees that developed it in this study was quite early, with 97% developing it by the end of the 1<sup>st</sup> week, and this compares well with the 75% reported within the few days postamputation by Krane and Heller.<sup>[17]</sup>

Assessment of pain intensity is considered one of the core outcome domains in clinical pain research, and the NRS is recommended.<sup>[24]</sup> The NRS used to rate pain intensity in this study is among the proven, valid, and reliable subjective methods of pain intensity measurement. It is unidimensional

and easy to use, with most patients demonstrating high compliance, sensitivity, responsiveness, and applicability compared to the Visual Analog Scale and Verbal Rating Scale.<sup>[25,26]</sup>

The participants with PLP in this study reported their greatest pain intensity as either mild (1–3 in the 11-point NRS) or moderate (4–6 in the 11-point NRS) during the course of our three observations, except two patient who had severe pain (7/10 and 8/10 in the 11-point NRS) within the 1<sup>st</sup> week postamputation period, with 55.7% having mild pain, 41.4% having moderate pain, and only 2.9% having severe pain. These NRS scores appear to be lower than the mean intensity of  $5.1 \pm 2.2$  and  $5.6$  reported by Yin *et al.* and Wartan *et al.*, respectively,<sup>[12,13]</sup> although pain intensity in each of their respondents was sampled only once. In the study by Yin *et al.*, 31.9% of the PLP sufferers had pain of severe intensity.<sup>[12]</sup> Similarly, in another retrospective cross-sectional survey utilizing a stratified sample of 914 American amputees, a mean pain intensity of  $5.5 \pm 2.6$  was reported by the PLP sufferers, with majority (38.9%)

reporting severe pain (7–10 in the NRS).<sup>[27]</sup> The study in an African population sample by Lacoux *et al.* also revealed a PLP pain intensity within the range of 2–6 (using the 11-point NRS) among the PLP sufferers, which is in the mild-moderate pain spectrum as in this study.<sup>[21]</sup> All the patients in the present study are Africans, and although the influence of race on pain intensity reporting has not been widely investigated, Mossey found that African Americans are more likely than non-Hispanic whites to underreport pain unpleasantness in the clinical setting, especially in the presence of physicians who were perceived as having “higher social status.”<sup>[28]</sup> The lower pain intensity reported in these two studies on African population samples in respect of PLP is, however, contrary to reports by Martinez *et al.*<sup>[29]</sup> and Creamer *et al.*,<sup>[30]</sup> indicating that compared with Caucasians, African American individuals report higher levels of pain for a number of similar chronic pain conditions including cancer and arthritis, respectively.

The most common descriptor of PLP in the study by Lacoux *et al.* was “stabbing,” followed by “pins and needles” with “burning” character reported infrequently.<sup>[21]</sup> The study by Wartan *et al.* similarly reported “stabbing” and “pins and needles” as the predominant descriptors with few “burning” type pain, whereas in our study, “biting” descriptor was most common, followed by “aching,” with “burning” being reported infrequently.<sup>[13]</sup> It would seem that the “biting” descriptor may be likened to “stabbing” used in different studies; much as the “pricking” may be likened to “pins and needles.” It could be observed that Lacoux *et al.*<sup>[21]</sup> and Wartan *et al.*<sup>[13]</sup> studied populations in which trauma was the indication for amputation in contrast to the present study which considered all limb amputations indicated by diverse pathology but whether this factor has any influence on the type of descriptor experienced by the amputees has not been evaluated.

We also observed that the course of the PLP changed remarkably over time with decreasing prevalence among the initial PLP sufferers and most patients having decreasing pain intensity. Three of the amputees in this study (4.3%), however, reported progressively worsening pain intensity even at 1 year postamputation. In the survey by Wartan *et al.*, PLP disappeared completely in 16% of the respondents reporting PLP, whereas intensity decreased substantially in 37%, remained the same in 44%, and even increased in 3%.<sup>[13]</sup>

### Factors associated with phantom limb pain

This study could not find any predictors of PLP among the amputees; hence, the knotty question persists. The amputees who were ASA Grade II were seven times more likely to experience PLP when compared with those who were classified as ASA Grade I and IV, but this was not statistically significant. This anesthetic index has not been considered in previous studies on PLP.

### Treatment of phantom limb pain

PLP is considered a neuropathic pain, and most current treatments are based on general recommendations for neuropathic pain syndromes as mechanism-based specific

treatment protocols recommended by Woolf and Mannion<sup>[31]</sup> are yet to evolve in view of the clinical challenge in determining which mechanisms may be operating in individual patients.

In this study, the treatment modality offered to the few treated PLP sufferers by their physicians was pharmacotherapy, consisting of diclofenac, paracetamol, carbamazepine, pregabalin, and chlorzoxazone. In a retrospective survey of 537 amputees in Germany, Kern *et al.* found that the vast majority of their PLP patients (71.1%) did not try any treatment, but among those who sought treatment, 30% consulted 4–20 physicians in search of beneficial treatment.<sup>[32]</sup> The magnitude of neglect and despair suffered by this subpopulation of amputees in both the Nigerian and German studies are reflections of the underrecognition and undertreatment of PLP across national frontiers. Another retrospective, questionnaire-based cross-sectional study involving American adult lower-limb amputees had revealed that pharmacotherapy was the most commonly used modality for PLP, with acetaminophen and opioids being most frequently used (both by 22% each), followed by nonsteroidal anti-inflammatory drugs (NSAIDs) (20%), even as acetaminophen and NSAIDs were rated to be of low helpfulness. Although nonpharmacological modalities were less frequently used: physical therapy (16%), massage (8%), transcutaneous electrical nerve stimulation (TENS) (7%), chiropractic care (4%), acupuncture (1%), and marijuana (1%), they were generally rated to be of moderate to high helpfulness.<sup>[33]</sup>

Similarly, in a survey of British amputees with PLP, the most frequently used pharmacotherapy was acetaminophen (53%) or an acetaminophen-opioid combination (37%), with more than 50% of the respondents each reporting satisfaction with the acetaminophen-opioid combination, NSAIDs, and alcohol, whereas the most common nonpharmacological therapy was TENS (36%), and 42% of the respondents who used TENS expressed satisfaction with this form of treatment.<sup>[13]</sup> New treatment approaches, such as mirror therapy which is simple and inexpensive, have been developed as a result of Ramachandran’s research using “virtual reality box”<sup>[34]</sup> and is promising.<sup>[35]</sup> A randomized controlled trial<sup>[36]</sup> found both mirror therapy and TENS to be effective in pain reduction on a short-term basis, but no difference was found between the two modalities of treatment. In spite of the multiplicity of interventions applied for PLP treatment, a 2017 review involving 38 currently used therapies concluded that no decisions can be made for the first-line management of PLP, as the level of evidence in favor of any therapy is too low.<sup>[37]</sup>

The paucity of literature on PLP in Nigeria is rather astonishing and negates the high rate of amputation in several published works in the country, and with the finding of high prevalence of PLP in this study, one may infer that a vast population of limb amputees in Nigeria and indeed Africa are suffering the PLP scourge, albeit silently.

It is noteworthy that most of the published works on PLP cited here, or otherwise, are retrospective and cross-sectional studies in which the pain was sampled at a single point in time

and different results may have been obtained if patient's pain was tracked over time, like in a prospective, cohort study as this. The latter method could also increase recovery rates and reduce dropout rate of the amputees leading to higher validity of the results.

### Limitations of the study

Beyond sensory intensity and perceptual quality of the PLP which were captured in the study, other important domains of neuropathic pain such as affect intensity (bothersome, anxiety, anger, depression, sleep disturbances, etc.) and temporal features (episodic, constant, fluctuating, etc.) could have been better captured with multidimensional pain assessment tools such as the McGill Pain Questionnaire and the Brief Pain Inventory, but these are rarely suitable in this clinical setting. Furthermore, actual PLP prevalence among the amputees in this study might have been underestimated since the cohort was followed up for only 1 year postamputation, whereas PLP onset may indeed be delayed for decades in some susceptible amputees, as revealed in a case report.<sup>[38]</sup>

### CONCLUSION

Despite scant mention in the regional literature, PLP is highly prevalent but untreated among limb amputees in Nigeria and indeed Africa. It is hoped that this modest effort will galvanize awareness and improved practice relating to PLP among health-care providers in Africa, considering the vast population of amputees in the region.

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### Conflicts of interest

There are no conflicts of interest.

### REFERENCES

- Dijkstra PU, Geertzen JH, Stewart R, Schans CP. Phantom pain and risk factors: A multivariate analysis. *J Pain Symptom Manage* 2002;24:578-85.
- Melzack R, Israel R, Lacroix R, Schultz G. Phantom limbs in people with congenital limb deficiency or amputation in early childhood. *Brain* 1997;120:1603-20.
- Thanni LO, Tade AO. Extremity amputation in Nigeria – A review of indications and mortality. *Surgeon* 2007;5:213-7.
- Okenwa WO, Eyichukwu GO, Nevo AC. Amputation of the limbs: 10 years' experience at Enugu State University Teaching Hospital. *Orient J Med* 2015;27:40-5.
- Ndukwu CU, Muoneme CA. Prevalence and pattern of major extremity amputation in a tertiary Hospital in Nnewi, South East Nigeria. *Trop J Med Res* 2015;18:104-8.
- Dabkana TM, Nyaku FT, Bwala ST. Current indications for extremity amputations in Maiduguri, North-East Nigeria: A 6-year retrospective review. *Ann Afr Med* 2018;17:22-5.
- Omoke NI, Nwigwe CG. Limb amputations in Abakaliki, South East Nigeria. *Afr J Med Health Sci* 2016;15:30-5.
- Agu TC, Ikwu AC. Any pattern changes in major lower limb amputations? A 10-year comparative retrospective study in a private orthopedic and trauma center in the South-East Region of Nigeria. *Niger J Gen Pract* 2017;15:1-6.
- Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract* 2011;94:311-21.
- Ajibade A, Akinniyi OT, Okoye CS. Indications and complications of major limb amputations in Kano, Nigeria. *Ghana Med J* 2013;47:185-8.
- Schans CP, Geertzen JH, Schoppen T, Dijkstra PU. Phantom pain and health-related quality of life in lower limb amputees. *J Pain Symptom Manage* 2002;24:429-36.
- Yin Y, Zhang L, Xiao H, Wen CB, Dai YE, Yang G, *et al.* The pre-amputation pain and the postoperative deafferentation are the risk factors of phantom limb pain: A clinical survey in a sample of Chinese population. *BMC Anesthesiol* 2017;17:69.
- Wartan SW, Hamann W, Wedley JR, McColl I. Phantom pain and sensation among British veteran amputees. *Br J Anaesth* 1997;78:652-9.
- Tian S, Nick S, Wu H. Phantom limb pain: A review of evidence-based treatment options. *World J Anesthesiol* 2014;3:146-53.
- Graham KZ, MacKenzie EJ, Ephraim PL, Trivison TG, Brookmeyer R. Estimating the prevalence of limb loss in the United States: 2005 to 2050. *Arch Phys Med Rehabil* 2008;89:422-9.
- Imam B, Miller WC, Finlayson HC, Eng JJ, Jarus T. Incidence of lower limb amputation in Canada. *Can J Public Health* 2017;108:e374-80.
- Krane EJ, Heller LB. The prevalence of phantom sensation and pain in pediatric amputees. *J Pain Symptom Manage* 1995;10:21-9.
- Jensen TS, Krebs B, Nielsen J, Rasmussen P. Immediate and long-term phantom limb pain in amputees: Incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain* 1985;21:267-78.
- Bosmans JC, Geertzen JH, Post WJ, Schans CP, Dijkstra PU. Factors associated with phantom limb pain: A 31/2-year prospective study. *Clin Rehabil* 2010;24:444-53.
- Kalauokalani DA, Loeser JD. Phantom limb pain. In: Crombie IK, editor. *Epidemiology of Pain*. Seattle: IASP Press; 1999. p. 143-53.
- Lacoux PA, Crombie IK, Macrae WA. Pain in traumatic upper limb amputees in Sierra Leone. *Pain* 2002;99:309-12.
- Aiyer R, Mehta N, Gungor S, Gulati A. A systematic review of NMDA receptor antagonists for treatment of neuropathic pain in clinical practice. *Clin J Pain* 2018;34:450-67.
- Zhou HY, Chen SR, Pan HL. Targeting N-methyl-D-aspartate receptors for treatment of neuropathic pain. *Expert Rev Clin Pharmacol* 2011;4:379-88.
- Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, *et al.* Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2005;113:9-19.
- Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, *et al.* Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: A systematic literature review. *J Pain Symptom Manage* 2011;41:1073-93.
- Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. *Pain* 2011;152:2399-404.
- Ephraim PL, Wegener ST, MacKenzie EJ, Dillingham TR, Pezzin LE. Phantom pain, residual limb pain, and back pain in amputees: Results of a national survey. *Arch Phys Med Rehabil* 2005;86:1910-9.
- Mossey JM. Defining racial and ethnic disparities in pain management. *Clin Orthop Relat Res* 2011;469:1859-70.
- Martinez KA, Snyder CF, Malin JL, Dy SM. Is race/ethnicity related to the presence or severity of pain in colorectal and lung cancer? *J Pain Symptom Manage* 2014;48:1050-9.
- Creamer P, Cejku ML, Hochberg MC. Determinants of pain severity in knee osteoarthritis: Effect of demographic and psychosocial variables using 3 pain measures. *J Rheumatol* 1999;26:1785-92.
- Woolf CJ, Mannion RJ. Neuropathic pain: Aetiology, symptoms, mechanisms, and management. *Lancet* 1999;353:1959-64.
- Kern U, Busch V, Müller R, Kohl M, Birklein F. Phantom limb pain in daily practice – Still a lot of work to do! *Pain Med* 2012;13:1611-26.
- Hanley MA, Ehde DM, Campbell KM, Osborn B, Smith DG. Self-reported treatments used for lower-limb phantom pain: Descriptive findings. *Arch Phys Med Rehabil* 2006;87:270-7.

34. Ramachandran VS, Ramachandran DR. Synaesthesia in phantom limbs induced with mirrors. *Proc Biol Sci* 1996;263:377-86.
35. Kim SY, Kim YY. Mirror therapy for phantom limb pain. *Korean J Pain* 2012;25:272-4.
36. Tilak M, Isaac SA, Fletcher J, Vasanthan LT, Subbaiah RS, Babu A, *et al.* Mirror therapy and transcutaneous electrical nerve stimulation for management of phantom limb pain in amputees – A single blinded randomized controlled trial. *Physiother Res Int* 2016;21:109-15.
37. Richardson C, Kulkarni J. A review of the management of phantom limb pain: Challenges and solutions. *J Pain Res* 2017;10:1861-70.
38. Rajbhandari SM, Jarratt JA, Griffiths PD, Ward JD. Diabetic neuropathic pain in a leg amputated 44 years previously. *Pain* 1999;83:627-9.