

## Original Article

# Prospect of Bone Xenograft as Alternate to Autologous Bone Graft: A Survey of Orthopaedic Surgeons Perspective in Nigeria

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## ABSTRACT

This study aimed at evaluating the problems associated with autografts in orthopaedic practice and the acceptability of alternative bone graft products to orthopaedic surgeons in Nigeria. Google form, an electronic questionnaire platform was designed and used for the purpose of this study. Orthopaedic surgeons in the designation of consultants and senior registrars were the respondents. Various questions were asked to know the complications associated with bone autograft and to deduce if locally available bone xenografts will benefit their practice. The data generated were analysed using descriptive statistics. A total number of 83 responses were received from this survey. This survey reported limited supply of autologous bone graft (83, 100%), donor site pain (77, 92.77%), donor site infection (44, 53.01%), haemorrhage (50, 60.24%) and prolonged duration of surgery (77, 92.77%) among other problems associated with harvesting bone autograft. Fifty-five (66.27%) responded that if the bone xenograft is prepared hygienically with consistency taking ethics and tissue rejection into consideration, it will circumvent the problems of autograft. We therefore conclude that efforts should be made toward research on how biocompatible bone xenograft could be locally prepared in developing countries that will be acceptable and affordable for orthopaedic practice to overcome the challenges of autologous bone graft and high cost of commercially available bone substitute.

**Keywords:** Autograft, bone xenograft, complication, fracture, orthopaedics

## INTRODUCTION

Most fractures are due to road traffic accident affecting more males than female.<sup>1,2</sup> Other causes include fall, gunshot, assault and pathologic fracture. The environmental conditions, demography and social economy are some of the factors that make aetiology of

fractures to vary within and among countries.<sup>3</sup> This invariably affects the particular bones fractured and fracture pattern. In low and middle income countries, 1000 to 2600 people sustain fractures out of 100,000 population per annum,<sup>2</sup> of which three percent will be an

open fracture.<sup>1</sup> In the United States, about six million fracture cases is recorded yearly and orthopaedic surgeries carried out involving the use of bone grafts was reported to be higher than half of a million.<sup>1,4</sup> This figure could be tripled when the entire world is considered, thereby making fracture a major public health concern.<sup>1,4</sup> Fracture healing of long bone diaphyses are sometimes impaired and result in delayed union or non-union or both which occur in about 10% of all fractures cases,<sup>5</sup> contributing to the reduced quality of life, significant treatment cost and considerable patient disability.<sup>6</sup> This brought about some therapeutic techniques to enhance the healing like the use of scaffold, demineralized bone matrix, cell therapies and parenteral drug administration.<sup>5</sup> To enhance bone healing in delayed union, non-union, malunion, arthrodesis, limb salvage, osteotomies, and to fill large defects because of fracture or removal of neoplasia or cysts, bone grafts are used.<sup>7,8</sup> Autologous bone graft remains the gold standard as it exhibits the best osteogenic potentials with no immunogenicity.<sup>4,7-10</sup> Autologous bone grafts are commonly harvested from the crest of the ilium.<sup>7,8,11,12</sup> Some other location include the proximal and distal part of the tibia, distal aspect of the radius and the greater trochanter of the femur.<sup>7,13</sup> Though Owoola *et al.*<sup>12</sup> and Salawu *et al.*<sup>8</sup> reported that the use of proximal tibia has advantages of reduced operative time, less haemorrhage, pain and donor site infection as opposed to the use of iliac crest. In harvesting autogenous bone graft, patients always experience some inconveniences. Infection and pain at the donor site, more surgical incisions, more haemorrhage, additional trauma, prolonged period of surgery and anaesthetic time with attending risks are some of the inconveniences. Furthermore, the donor bone is also weakened and the normal structure is sacrificed, aside possible nerve and vascular injuries.<sup>12</sup> Complications associated with autologous bone grafting could occur during surgery, acutely or chronically post-surgery and could occur at the augmented or donor site.<sup>9</sup> Goulet *et al.*<sup>11</sup> reported catastrophic complications, though rare, in a retrospective assessment of orthopaedic surgeries involving use of bone grafts. The complications

are related to the closeness of the site to neurologic and vascular structures and include arteriovenous fistula, hernia, ureteral injury, pelvic vasculature pseudoaneurysm, neuropathy and low back pain due to pelvic instability. Other complications include patient discomfort, cutaneous nerve damage, compromised cosmetic appearance of the donor's incision site,<sup>11</sup> donor site infection, haematoma, iatrogenic fracture,<sup>7,14</sup> dehiscence of soft tissue and at worst, failure of graft 'take'.<sup>9</sup> In addition to all these complications, autologous donor sites have limited supply of graft in terms of quantity, require additional time for harvesting thereby prolonging duration of surgery, prolong hospital stay and may be difficult to access.<sup>4,7,8,10</sup> These limitations ignited researchers and clinical trials to seek alternative bone graft sources which brought the like of allograft, xenograft and bone biomaterials in their different forms into limelight.<sup>15</sup> Bone allograft is another alternative harvested from human cadaveric donors.<sup>13</sup> It is available in many processed forms, but poses the risk of transmission of infections and could only serve as a scaffold because the procedures of sterilizing and storing them would have destroyed the innate osteogenic and osteoinductive properties.<sup>4,14,16</sup> Allografts have some advantages over autografts as it could be made available from an unlimited sources, it reduces the operative time and is not associated with donor site morbidity.<sup>16</sup> The risk of transmitting infections especially viral,<sup>17</sup> immune and inflammatory responses post-implantation<sup>18,19</sup> and increased demand for bone reconstruction had led to a relative deficiency in allogeneic donors as well.<sup>4</sup> The disadvantages of both autograft and allograft intensified the research into finding other bone substitutes.<sup>4,20</sup> Xenografts of solid organs have been a successful phenomenon though plagued due to extreme limited number of suitable donors.<sup>21</sup> This limited number of xenodons is however not the case for bone grafts as bones for some domestic animals<sup>15,22-24</sup> and aquatic animals<sup>25</sup> have been tested and commercialized. Among the most frequently used bone xenograft is sourced from bovine because they have structure and chemical composition similar to that of human bone with

good osteoconductive properties and adequate rate of resorption.<sup>22</sup> In addition, they are always readily available and cheap.<sup>22,26</sup> Many success have been recorded when bovine bone xenograft was used to manage varying types of bone defects.<sup>22,27</sup> Furthermore, bovine bone collagen induces ingrowth of vessels, deposition of minerals, and growth factors binding, it is therefore a good material in bone tissue regeneration and repair.<sup>22</sup> Of more interest and advantage is the bovine cancellous bone xenograft because they are biologically porous and thereby enhances invasion of both cells and vessels.<sup>15</sup> The best example of osteoinductive xenograft material is the bovine demineralized bone matrix (DBM) as it initiates production of osteoblasts from the mesenchymal cells.<sup>22</sup> The antigenic properties of the bone is also reduced and the bone matrix is made available and bioactive for local cells differentiation upon demineralization.<sup>22</sup> Many growth factors have been reported to be present in extracellular collagen matrix of DBM which are responsible for its osteoinductive properties. These include fibroblast growth factor, insulin-like growth factor, bone morphogenetic proteins (BMPs) and transforming growth factor beta.<sup>22</sup> Bone xenograft could therefore be a good alternative to autografts and allograft as it circumvents some of the complications attached to them.

The cost of management is also an important factor to be considered as a large percentage of Nigerians live below \$1 per day.<sup>2</sup> Cost of management of non-union fractures in the United Kingdom, for example, was estimated to be between £7000 and £79000 for the hospital treatment only while \$25,556 USD was estimated for the management of the same condition in the United States with increased administration and longer duration of opioids.<sup>6</sup> With these large initial cost estimates, additional costs of bone grafts substitutes have to be minimal in a country like Nigeria with limited health insurance facilities. Therefore, an alternative cheap and affordable source of bone graft that will avoid an additional surgical site, possible donor site morbidity and will reduce hospital stay should be made available.

We therefore study the perspective and acceptability of

local bone xenograft among orthopaedic surgeons in Nigeria through a survey, taking into cognisance the current challenges with the use of autografts and the expensive nature of commercially available bone biomaterials.

## MATERIALS AND METHODS

Nigerian orthopaedic surgeons within the designations of Senior Registrar and Consultants were the respondents of this survey. A Google survey was conducted which was sent through electronic means to the surgeons. The consent of the surgeons that participated in this survey was sought. The questionnaire was structured into two parts: practice information and fracture management, bone graft usage and cost implication. The practice information included the type of establishment, designation and years of orthopaedic practice. In the second section, the respondents were asked about the average case load per month, the most affected gender and bone, availability of bone bank, most frequently used bone graft, awareness and use of bovine bone xenograft, cost of fracture management with or without grafting, challenges associated with the use of autograft and if locally available bone xenograft will benefit their practice amongst other questions. The data generated from the responses were analyzed using a descriptive statistics.

## RESULTS

A total of 83 responses were received from this survey among which 57 (68.67%) and 26 (31.33%) were from Teaching and Specialist Hospitals respectively. The designations of the respondent were Consultants (64, 77.11%) and Senior Registrars (19, 22.89%) with various years of practising experience (Fig.1). On average monthly, 11 (13.25%) of the respondents reported that they manage up to five orthopaedic and trauma cases requiring open reduction while 39 (46.99%), 27 (32.53%) and 6 (7.23%) reported 11-15, 21 and above, and 16-20 cases respectively. Seventy-one (85.54%) respondents responded that males are more affected and the remaining

12 (14.46%) said they receive such cases in the same proportion between male and female.

The femur is the most frequently fractured bone seen as 42 (85.54%) of the respondents reported. Other frequently affected bones were tibia and humerus as reported by 28 (33.73%) and 6 (7.23%) and respondents respectively. Seven (8.4%) of the respondents reported that the affected bones vary monthly among femur, humerus, tibia and radius/ulna. All the respondents (100%) responded that there is no bone bank in their establishments. They all responded that autograft is always available as the most frequently used graft when the need arises and 11 (13.25%) of the respondents said there are bone biomaterials available for them to use. These autografts are commonly harvested from the iliac crest (39, 46.99%) and in the same proportion between iliac crest and proximal tibia (44, 53.01%).

Fig. 2 shows the responses on which animal is known to be closest to humans in terms of bone structure for the possibility of being a bone xenograft source. On alternative to autograft, 62 (74.70%) answered in affirmation that they are aware of commercially available bovine bone xenograft while 7 (8.43%) had ever used it. On the cost of artificial bone graft substitutes in Nigeria, 34 (40.96%) responded that they have idea of the prices which is in the range of N35,000 to N70,000 (approximately \$91 - \$181) which posed an additional cost to the surgery. Bone grafts are used for several reasons and in different situations, the respondents however responded that they would use bone graft due to challenges with bone healing (82, 98.80%), presence of large defect (69, 83.13%), and to enhance joint arthrodesis (6, 7.23%).

Challenges with harvesting, post-surgical pains, quantity limitation, bleeding, donor site infection, iatrogenic fracture, cosmesis and time of harvest were the challenges associated with the use of bone autograft according to the respondents (Fig.3). Fig.4 showed the reasons why orthopaedic surgeons will want to opt for another source of bone graft aside autograft. The respondents were asked if locally available xenograft will benefit their practices, 55 (66.27%) responded that it will

benefit their practices while 28 (33.73%) were of the opposite opinion. Those that responded that locally available xenograft will benefit their practices gave reasons that: there will be more grafts available to bridge large defect (50.60%); there will be no problem of site morbidity and the hospital stay is reduced (46.99%); it can be used as scaffold (6.02%); and its possible affordability (7.23%). On the other hand, 5 (6.02%) respondents categorically responded that bone xenograft has no application while others will consider ethical issues (4.82%) and acceptability (8.43%) before using it.

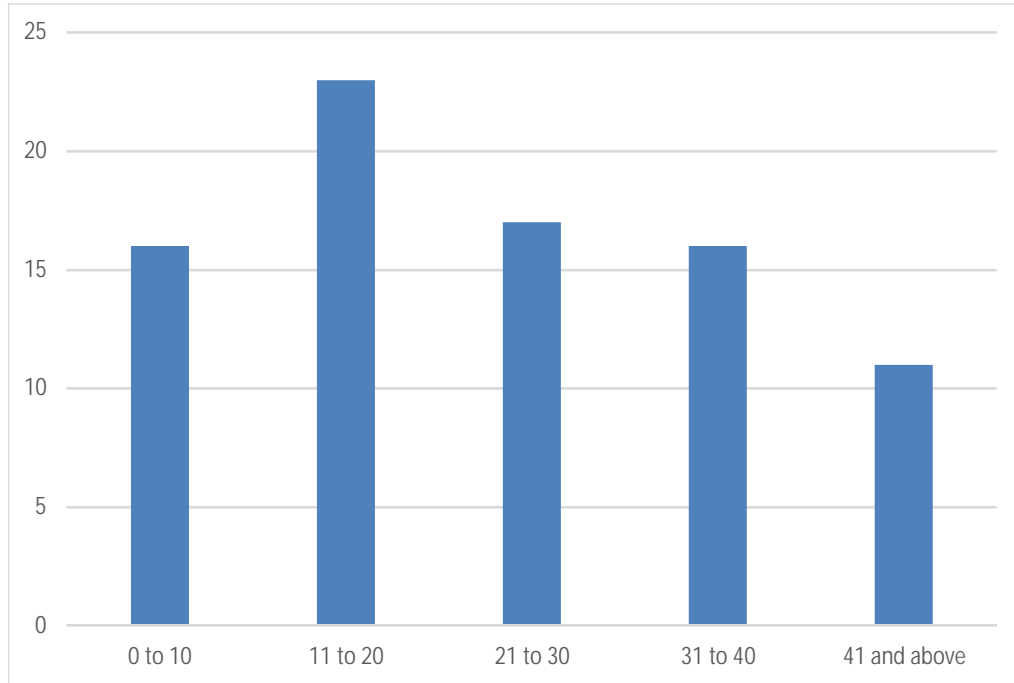


Fig. 1: Years of Practice of the respondents and their corresponding numbers

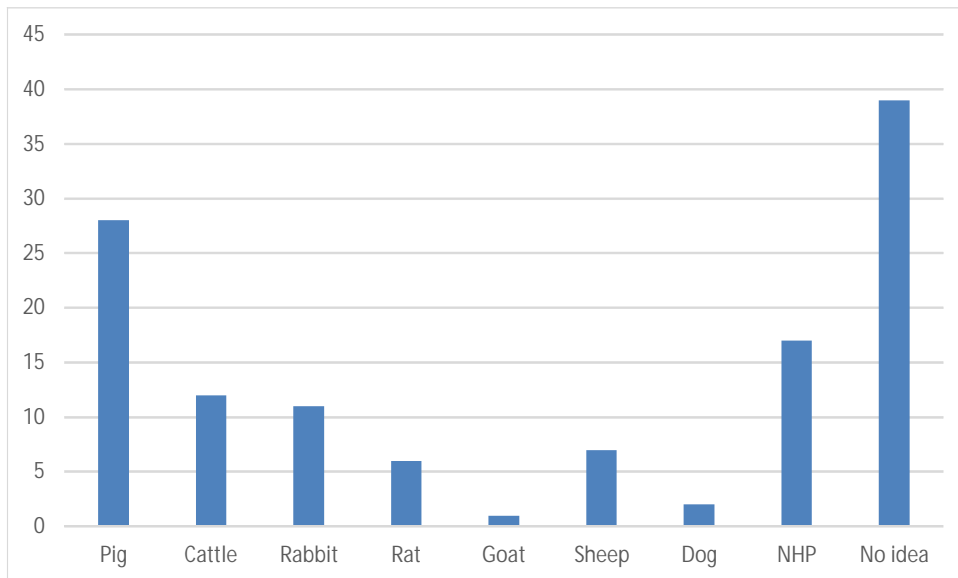


Fig 2: Respondents opinion about the species of animal known to be closer to human in terms of bone structure.  
NHP: Non-human primates

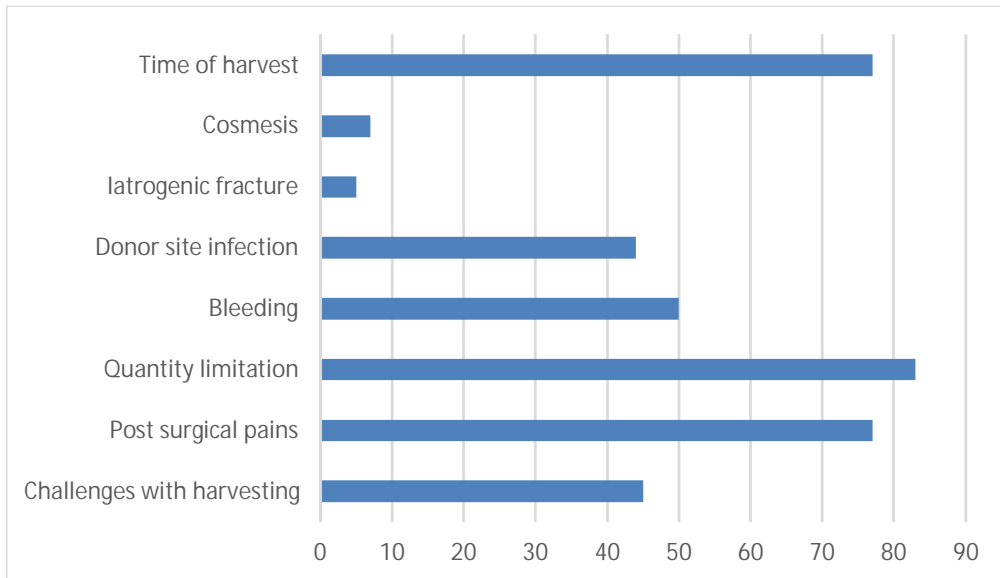


Fig 3: The responses on the challenge of autograft based on the opinion of the respondents

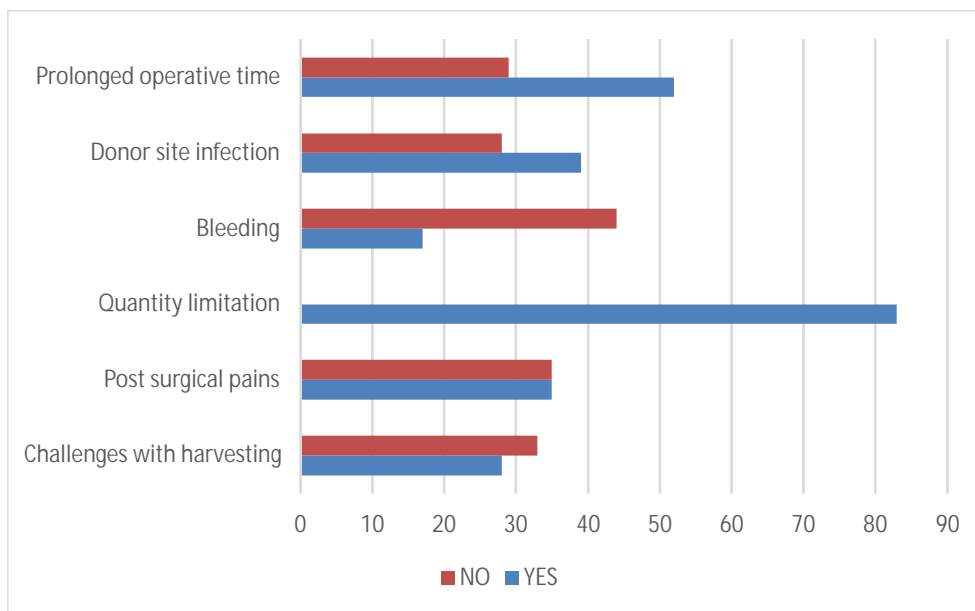


Fig 4: Respondents opinion on the reasons why alternate source of graft will be opted for aside autograft

## DISCUSSION

Healing of long bones diaphyseal fractures is challenging and 10% of the cases could result in delayed or non-union fractures which could reduce the quality of life, increased significant treatment cost and considerable patient disability.<sup>5,6</sup> This is of economic importance as it affects largely the industrious agile people in working age group.<sup>2</sup> These challenges brought about some therapeutic techniques to enhance the healing like the use of scaffold, demineralized bone matrix, cell therapies and parenteral drug administration.<sup>5</sup> Bone grafts are used to enhance bone healing in new fracture cases to fill large defects, delayed union, non-union, malunion, arthrodesis, limb salvage and ostectomies.<sup>7,8</sup>

This study revealed the challenges associated with bone autografting as it has been reported in other part of the world with readiness to accept and use alternative source of bone graft like xenograft if it could be made available in a cheap, acceptable and sterile manner. To have unbiased responses and to make substantial inference, the survey was conducted among the consultants (71.11%) and senior registrars (22.89%) that handle orthopaedic cases in Teaching (68.67%) and Specialist (31.33%) hospitals. The highest average caseload requiring bone graft per month ranged from five to above 21 cases per month. This variation in number depends on demographic and socioeconomic factors in the area of practice.

In accordance with the present study, males have consistently been reported to be the most affected gender in terms of fracture,<sup>1,5</sup> perhaps due to the daily engagements, hard and laborious works and attempts to feed the family. Babalola *et al.*<sup>2</sup> and Odatuwa-Omagbemi<sup>1</sup> reported that tibia and fibula were the most frequently affected bones followed by the femur which was in contrary to the present study as femur was reported to be the most affected bone as 42 (85.54%) respondents reported femur as the most affected bone followed by tibia 28 (33.73%) respondents. The areas where the survey was conducted and the fact that the direction of the trauma and the protective attempt of the individual victim

could cause the variation in the most affected bone. Our findings on most affected bone was however inconsistent with the review of 422 fracture patients by Admasie *et al.*<sup>28</sup> in Ethiopia who reported a higher frequency of fracture on the femur (68, 15%), just as we observed in the current study.

It was observed in this study that many orthopaedic surgeons are used to autograft unlike other sources, despite the complications associated with it. Our finding is in line with the conclusion of the review of Marongiu *et al.*<sup>5</sup> which showed a strong evidence for the use of bone autografts in healing enhancement. This could be as a result of the technical-know-how, ready access to limited quantity of autografts, cost of substitutes and fear of immune reactions from the substitutes. The most commonly used donor site is the iliac crest followed by the proximal tibia.<sup>8,12</sup> This is in accordance with the findings in the current study as 39 (46.99%) of the respondents commonly use the iliac crest while 44 (53.01%) of the respondents use the iliac crest and proximal tibia in the same proportion. This is despite the fact that some authors reported reduced pain, operative time, haemorrhage and donor site infection with proximal tibia as compared to the iliac crest.<sup>8,12</sup> Eighty-two (98.80%) respondents primarily use bone grafts when there are challenges with bone healing. These challenges include delayed union, non-union and mal-union. Other indications as observed include filling of large defects and arthrodesis reported by 69 (89.13%) and 6 (7.23%) respectively. This observation is in agreement with the reports of Owoola *et al.*<sup>12</sup> and Salawu *et al.*<sup>8</sup> that challenges with bone healing is the commonest indication of bone grafting followed by defect filling and arthrodesis enhancement.

The respondents in this study reported that the commonest challenges with bone autograft and why alternate source is necessary was the quantity limitation (83, 100%) followed by the prolonged operative time and post-surgical pains, both were reported by 77 (92.77%) respondents. Other reasons were due to haemorrhage (50,

60.24%), challenges with harvesting (45, 54.22%), donor site infection (44, 53.01%), cosmesis (7, 8.42%) and iatrogenic fracture (5, 6.02%). All these complications have been previously reported and choice of which is considered most relevant is dependent on the technical-know-how of the surgeon, the case to be managed, available resources, economic status of patients and area of practice.<sup>7,11,12</sup>

In the search of an alternative to autograft, it was observed that only bone biomaterial was reported to be available aside autograft as reported by 11 (13.25%) of the respondents while there were no responses for allografts and xenografts. This tallied with the response of non-availability of bone bank by all the respondents as it is majorly allografts and xenografts that should be in the bone bank. Culture, ethics and religious belief of Nigerians may not favour having bone bank stocked for allograft, because there may not be anyone who will willingly consent to donate his or her bones after death or the relatives of the corpse may not allow harvesting of the bones. The cost of artificial grafts and biomaterials available are in the range of N35,000 to N70,000 (approximately \$91 - \$181) as reported by 62 (74.70%) of the respondents. This will be an additional cost to the patients in a country of N30,000 (\$78) minimum wage with a large percentage of the population living below \$1 per day and with limited health insurance cover.

Fifty-five (66.27%) of the respondents said locally available bone xenograft will benefit their practice as there will be sufficient amount of bone graft available to bridge large defect, avert the problem of donor site infection, reduce hospital stay and will be available at cheaper price. On the other side, 28 (33.73%) responded that bone xenograft will not benefit their practice putting ethical issue and acceptability into consideration. Having no previous contact or awareness of commercially available bovine and coral fish bone xenograft might have made them to be of the perspective that bone xenograft, if made locally, will not benefit their practice, and avert largely the challenges associated with bone autograft.

## CONCLUSION

There are challenges associated with the bone autograft in Nigeria as reported by the respondents in this study. The challenges which mostly border on limited supply in terms of quantity, post-surgical pain and donor site infection. As bone xenograft has benefitted orthopaedic practice in other parts of the world, responses from Nigerian orthopaedic surgeons have largely supported conducting research to make xenograft a promising substitute. This will have an added advantage of being available in large quantity at a relatively affordable cost for the average Nigerian. It is therefore recommended that efforts should be made towards local preparation of viable bone xenograft in Nigeria, that will be easily accessible, available and cheap for all patients regardless of economic class.

## Conflict of Interest

The authors declare that there is no conflict of interest.

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