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Functional and radiological outcomes of atypical femur fractures among elderly in Karachi, Pakistan

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Introduction
Over 200 million people suffer from osteoporosis worldwide and is considered as a major health concern. Osteoporosis is considered to be the 2nd most critical health problem by the World Health Organization. In Pakistan the prevalence of osteoporosis is suggested to be 9.1 million and it is further estimated that this figure was projected to rise by 11.3 million by the year 2020 overburdening an already resource constrained environment. These figures suggest a major burden of osteoporosis in health sector of Pakistan. Bisphosphonates have been the first line therapy for management of osteoporosis for the past 20 years. They reduce osteoclastic bone resorption and the net result is a rapid and substantial decrease in bone turnover markers resulting in a modest increase in bone mineral density (BMD). It has been proposed that severe and prolonged suppression of bone turnover may impair the ability of bone re-modelling leading to an accumulation of micro damage and reduction of bone strength resulting in iatrogenic fractures.

Atypical femoral fractures (AFFs) are defined as atraumatic or low-energy trauma fractures located in the sub-trochanteric region or femoral shaft. Patients usually present with a history of prodromal pain in the affected thigh, months prior to the actual injury which should prompt a physician to ask specifically for bisphosphonate use and then correlate with the radiology. Radiological features of AFFs are unique and include a simple transverse pattern with a uni-cortical break in an area of cortical hypertrophy. The diagnosis of AFFs specifically excludes femoral neck fracture, high impact trauma related fractures, pathological fractures associated with primary or secondary tumours, intertrochanteric fractures, and peri-prosthetic fractures. American Society for Bone and Mineral Research (ASBMR) has devised criteria for diagnosing an atypical fracture with major and minor features. Few drugs like bisphosphonates, glucocorticoids, proton- pump inhibitors and medical conditions such as diabetes, rheumatoid arthritis and vitamin D deficiency are included in the minor criteria. Understanding the scarce literature and need for evaluation of these fractures this study was carried out for better understanding of the outcomes of surgically managed AFFs.

Materials and Methods
This study was a retrospective observational study conducted at Aga Khan University Hospital, Karachi,
Pakistan after the institutional ethics review committee approval (ERC# 4759-Sur-ERC-17). Patients who were diagnosed for AFFs according to the ASBMR criteria and surgically managed with intra medullary nail between January, 2013 to June, 2017 were included in this study and data was analyzed after final follow-ups of all patients in December 2019. Sample size was calculated via WHO sample size calculator tool estimating population proportion of 0.98 with absolute precision required of 0.06, the sample size required for the study was 21 patients. We included 24 patients in our study. Patient's demographic data including age, gender, occupation, duration of previous bisphosphonate use, mechanism of injury, fracture site of femur either sub-trochanteric or femur shaft, duration of surgery and post-operative use of bone remodeling agents were collected from the patients’ charts and recorded on a preformed structured proforma. Serial radiographs were viewed to ascertain the fracture healing and consolidation on regular follow-ups. Patients were followed for a minimum period of 24 months post operatively. Short Musculoskeletal Functional Assessment (SMFA) score was calculated via telephonic interview after verbal consent and used to assess the functional outcome of patients with a lesser score indicating better outcome. Categorical variables were recorded as frequency and percentages and chi-square test or Fischer exact test was applied for analysis. Continuous variables were expressed as means with standard deviation. Data was checked for normality via Shapiro-Wilk test and student t-test was applied to compare means for analysis. A p-value of less than 0.05 was considered significant for inferential analysis. Statistical package for the social sciences (SPSS) version 20 was used for all analysis.

Results

A total of 24 patients were included in this study of whom 21 were females and 3 were males. Mean age of the patients was 65.5±8 years. Majority of the patients sustained ground level fall. Twenty (83.3%) fractures occurred in sub-trochanteric region while 4 (16.7%) were femoral shaft fractures. Five patients out of 24 (20.8%) had a history of steroid use. Twenty-two patients took bisphosphonates for osteoporosis while 2 patients had never used them. Mean duration for bisphosphonates usage was 6.4±1.3 years. None of the patients took any other medication for osteoporosis prior to the fracture. Six patients reported a history of prodromal thigh pain with a mean duration of 1.6±0.7 months (Table-1).

All the patients were surgically managed with intramedullary nailing device (Figure-1 & 2). Mean duration of hospital stay was 6.75 ±2.3 days. Mean time for fracture healing was 10.8 ± 3.2 months. Five (20.83%) patients had dynamization of nail 3 months after index surgery. Two (8.3%) patients underwent additional procedures at 5th and 7th month respectively due to delayed union and were subjected to bone grafting. Both patients healed after 4 months of second surgery. All the patients reported a good score on SMFA with mean 26.29% ± 2.89 (range 19% to 31%). Mean follow up time was recorded as 26.4±2.75 months (Range 24-35). All the patients stopped using bisphosphonate after surgery.

Interestingly accelerated fracture healing was associated with use of osteoblastic agents like Strontium Ranelate and Teriparatide which was given to the patients as per surgeons' discretion. Patients who used any osteoblastic supplements post operatively showed a better mean healing time of 7.2 ± 2 months while mean healing time of 12.7 ± 3.3 months was observed in those patients who were not prescribed any agent (p=0.008). Eleven patients were prescribed Strontium Ranelate as per treating surgeons’ discretion while 6 used Teriparatide as osteoblastic agents. Patients using Strontium had a mean healing time of 7.36±2.1 months while for Teriparatide group it was 7.0±2 months. Comparison of Strontium and Teriparatide using patients and mean healing time was not found to be statistically significant (Table-2).

### Table-1: Patient demographics and fracture characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean/Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>65.5±8.0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3 (12.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>21 (87.5%)</td>
</tr>
<tr>
<td>Steroid Use</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (20.8%)</td>
</tr>
<tr>
<td>No</td>
<td>19 (79.2%)</td>
</tr>
<tr>
<td>Prodromal Pain</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6 (25%)</td>
</tr>
<tr>
<td>No</td>
<td>18 (75%)</td>
</tr>
<tr>
<td>Fracture location</td>
<td></td>
</tr>
<tr>
<td>Sub-trochanteric</td>
<td>20 (83.3%)</td>
</tr>
<tr>
<td>Femur shaft</td>
<td>4 (16.6%)</td>
</tr>
</tbody>
</table>

### Table-2: Stratified healing times according to osteoblastic agents.

<table>
<thead>
<tr>
<th>Use of Supplement</th>
<th>Mean (months)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (n=17)</td>
<td>7.24±2.0</td>
<td></td>
</tr>
<tr>
<td>No (n=7)</td>
<td>12.71±3.3</td>
<td>0.08</td>
</tr>
<tr>
<td>Strontium (n=11)</td>
<td>7.36±2.1</td>
<td></td>
</tr>
<tr>
<td>Teriparatide (n=6)</td>
<td>7.00±2.0</td>
<td>0.73</td>
</tr>
</tbody>
</table>

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Atypical femurs are not uncommon but still are tricky to pick and require prompt careful history taking and assessment. The mechanism of action and fracture pattern on radiographs are the key to correct diagnosis. Our study delineates various aspects of assessment including specific questions while taking history such as prodromal pain, bisphosphonates use and its duration.

The association between long-term bisphosphonate use and unusual diaphyseal fractures was first described in 2005 by Odvina et al.13 Many studies have documented this association14 while according to Rizzoli et al, this case is yet unproven.15 For the past 2 decades, bisphosphonates have been the main stay treatment for the prevention of osteoporosis related fractures. In year 2005, it was reported that prolonged use of BP has association with an unusual diaphyseal fracture and later it was termed as atypical femoral fracture by ASBMR.16 The first report from the ASBMR task force published in 2010 showed lack of studies regarding management and outcomes for atypical femoral fractures.10

Egol et al. had reported a good outcome of surgically managed atypical femoral fractures with 98% of fractures healing at 12 months, and 60% becoming pain free post-operatively11 whereas in our study, mean healing time was 10 months. Ha et al. studied the necessity of surgical management for atypical femoral fractures and their study population reported a 100% healing rate after surgical fixation17 which is comparable to our study.

A case series of 21 patients of atypical femoral fractures showed a positive relation with smoking and steroid use while all the fractures were managed with intra medullary nailing and only one had non-union and rest healed uneventfully.18 In our study none of the selected patients had history of smoking and 5 patients used steroids. There was no significant relationship found for the usage of steroids or cigarette smoking.

Ekstrom et al reported 25% mortality at 2 year follow-up in patients managed surgically for atypical femoral fractures, while 52% did not achieve the pre-fracture quality of life.19 There were no reported mortality of subjects in our study. In our data the SMFA scores were reported to be good in patients with early healing time. High scores were encountered in patients with delayed union or who underwent additional procedures. Weil et.al conducted a study which showed much higher failure rates with intra medullary nailing for atypical femoral fractures and requiring revision surgery, 54% achieved fracture healing while 46% had to undergo a revision surgery.20 Subramanian et.al reported a good surgical outcome for atypical femoral fractures with all the patients having uneventful healing while only one fracture developed non-union requiring revision surgery.18 Our study results showed that only two patients had to undergo redo surgery due to non-union after initial management but later achieved union.

There were no studies found to have comparison between usage of post-operative supplements like
Teriparatide and Strontium. In our study we found an association between early fracture healing with use of osteoblastic drugs warranting better SMFA as compared to those who did not use it. Since this was an observation, further studies are required to look in this association more closely.

The strengths of the study is its adequate follow up period to delineate union and occurrence of any re-fracture. Moreover it provides an association between use of osteoblastic agents and healing time. The limitations of our study were a small sample size, its retrospective nature, and the functional outcome assessed over a telephonic interview.

**Conclusion**

This study reported comparatively good outcome for patients with atypical femoral fractures when managed with intra-medullary nailing. Use of post-operative osteoblastic supplements showed statistically significant results with early healing time, hence warranting further prospective studies and randomized controlled trials to study the relationship and association of Teriparatide or Strontium Ranelate with healing after surgical management.

**Disclaimer:** The study was conducted after approval of institutional Ethical review committee and informed verbal consents from the patients.

**Conflicts of Interest:** The authors declare that they have no conflict of interest.

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**References**