Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(2A):311-315 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i02.005

Original Research Article

Survey on pathologic fractures over a 10-year period from 2005-2015 in Yazd, Iran

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Abstract: Pathologic fractures refer to bone fractures caused by different diseases and a subsequently weakened bone structure prone to fractures by the slightest trauma and sometimes even no trauma at all. Finding the underlying factors contributing to a condition comprises a major goal of health systems in different societies. The present retrospective study was conducted on all the patients with a fracture sample sent to the pathology department of Shahid Sadoughi Hospital of Yazd between late January 2005 and late May 2015 selected through simple random sampling. The patients' demographic information, including age, gender, site of fracture, cause of fracture, underlying diseases and pathological results, were recorded in a pre-formulated checklist and then analyzed in SPSS version 17. P-values less than 0.05 were considered statistically significant. Of the total of 100,000 cases referred to the pathology department of the select hospital over the 10-year period, 64 cases were related to pathologic fractures. About 56.3% of the cases of pathologic fracture were male and 43.7% female. Of the 64 cases, 24 (37.5%) had avascular necrosis, 15 (23.4%) osteoporosis, 9 (14.1%) bone metastases, 5 (7.8%) bone cysts, 7 (10.9%) inflammatory reactions and 4 (6.3%) primary bone tumors. A significant relationship was observed between the site and cause of fracture and the patients' age ($P<0.05$). The present study found pathologic fractures to be highly prevalent among patients with avascular necrosis and osteoporosis, given that avascular necrosis was the most frequent cause of pathologic fractures among the younger and osteoporosis among the older individuals.
Keywords: Fracture, Bone, Avascular necrosis, Osteoporosis.

INTRODUCTION

Pathologic fractures refer to bone fractures caused by different diseases and a subsequently weakened bone structure prone to fractures by the slightest trauma and sometimes even no trauma at all [1, 2]. The main localized diseases causing pathologic fractures include chronic osteomyelitis, enchondroma, simple bone cyst, Ewing's sarcoma, metastatic carcinomas (such as lung, breast, kidney and prostatic origin) and osteoporosis [3, 4]. Common diseases causing pathologic fractures include congenital disorders characterized by poor ossification (such as osteogenesis imperfecta and fibrous dysplasia), reduced bone quality (such as avascular necrosis and osteomalacia), tumors (such as multiple myeloma), Gaucher's disease and osteoporosis due to diseases such as hyperthyroidism, Cushing's disease, rickets, renal rickets and gastrointestinal diseases such as celiac, steatorrhea and malnutrition and senile osteoporosis [1-4]. Pathologic bone fractures are diagnosed by radiography and through clinical examinations and comprise one of the main reasons for removing a part of the bone [5]. Osteoporosis is one of the most prevalent causes of pathologic fractures. Osteoporosis and subsequent fractures form a serious problem in the aging population of countries [6, 7]. These fractures impose high treatment costs on the healthcare system in addition to reducing the patients' quality of life and putting their relatives under a lot of mental pressure [7, 8]. In one study, Kevin P. Chang showed that almost half of hip fractures occurred before the age of 80 in men and two third of them before the age of 85 in women; the age distribution of hip fractures in this study indicates the importance of early osteoporosis interventions [9]. Malnutrition is one important cause of pathologic fractures in many countries, including in parts of Iran [10]. Some other causes of pathologic fractures include metastatic cancers originating in the breast, lung, prostate, gastrointestinal tract, etc., which weaken the bone tissue and cause pathologic fractures [2, 3]. The number of patients with these conditions is increasing across the world, including in Iran. The present study was conducted in response to the growing aging population of Iran and since a substantial

percentage of the causes of pathologic fractures can be prevented. Given that determining the cause of fractures contributes to the effectiveness of therapeutic interventions, the researchers decided to carry out a clinicopathological study of pathologic fractures during the past ten years in Yazd, Iran.

MATERIALS AND METHODS

The present retrospective study was conducted on all registered patients presenting to Shahid Sadoughi Hospital of Yazd between late January 2005 to late May 2015 for pathologic fractures and undergoing biopsy. The samples were selected through the census method. Patients with a bone fracture caused by car accident trauma, falling from heights, or sports injuries were excluded from the study. The patient's informations such as age, gender, site of fracture, year of fracture, pathological diagnosis and causes of fracture were extracted from their pathology and hospital records according to the prepared checklist. The study protocol was approved by the ethics committee of Shahid Sadoughi University of medical sciences, Yazd, Iran. Data were analyzed using SPSS software, version 17 for windows (IBM Inc., NY, US). Fischer's exact test was used as appropriated. P-values less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

Of the total of 100,000 cases referred to the pathological department of the select hospital between late January 2005 and late May 2015, 64 cases had pathologic fractures, 36 (56.3%) of whom were male and 28 (43.8%) female. The youngest patient examined was 14 and the oldest 87. The mean age of the patients was 55.64±21.63 (mean±SD) years. Of the 64 cases of pathologic fracture, 24 cases (37.5%) had avascular necrosis, comprising the most frequent pathology, while 4 cases (6.3%) had primary bone tumors, comprising the least frequent pathology (Table 1). The study population was divided into four age groups: below 30, 30-50, 50-70 and over 70. The frequency distribution of the pathological results of the study was examined in the four age groups. Avascular necrosis, which was the most frequent cause of pathologic fractures in the present study, was most common in the 30-50 age groups with a frequency of 45.8%. Osteoporosis, however, was most frequent in the over 70 age group with a frequency of 60%. The 50-70 age groups contained 55.6% of the cases of pathologic fracture caused by bone metastases. All the 5 cases of bone cyst belonged to the below-30 age group, while 57.1% of the cases of inflammatory reaction belonged to the over-70 age group and 75% of the cases of primary bone tumor belonged to the 50-70 age group. Significant relationship was found between the patients' pathological results and the age (P=0.001). The femur was the most common anatomical site of fracture with a frequency of 84% (n=54). 100% of the cases of avascular necrosis and the majority of the cases of osteoporosis (66.7%) were found in the femur. The femur was the most common bone fractured due to bone metastases with a frequency of 88.9%. A total of 80% of the cases of bone cyst in the femur (n=4) and 20% of the cases bone cyst (n=1) in the radius resulted in pathologic fractures. Of the 7 cases of inflammatory reaction, the femur was the most common site of fracture with a frequency of 71.4% (n=5). A total of 75% of primary bone tumors (n=3) were found in the femur, resulting in pathologic fractures (Table 2). Significant differences was obtained between the patients' pathological results and the anatomical site of fracture (Fisher's exact test, P=0.004).Table 3 presents the frequency distribution of the pathological results of the study in terms of gender; however, Fisher's exact test shows no significant differences between the patients with respect to this variable (P=0.460).

Table 1: Frequency distribution of bone fractures based on pathology findings, N=64

Pathology results	Number	%
Avascular necrosis	24	37.5
osteoporosis	15	23.4
Metastasis	9	14.1
Bone cyst	5	7.8
Inflammatory reactions	7	10.9
Primary bone tumor	4	6.3

Table 2: Frequency distribution of pathology results based on location of fracture

Location of fracture	Pathology findings						
	Avascular necrosis N (%)	Osteoporosis N (%)	Metastasis N (%)	Bone cysts N (%)	Inflammatory reaction N (%)	Primary bone tumor N (%)	Total N (%)
Pelvic	0 (0)	1 (6.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.6)
Femur	24 (100)	10 (66.7)	8 (88.9)	4 (80)	5 (71.4)	3 (75)	54 (84.4)
Vertebra	0 (0)	4 (26.7)	0 (0)	0 (0)	1 (14.3)	0 (0)	5 (7.6)
Tibia	0 (0)	0 (0)	1 (11.1)	0 (0)	1 (14.3)	0 (0)	2 (3.1)
Humerus	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	1 (1.6)
Radious	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	1 (1.6)
Total	24 (100)	15 (100)	9 (100)	5 (100)	7 (100)	4 (100)	64 (100)

Fisher's exact test, p-value<0.05

Table 3: Frequency distribution of pathology findings based on patient's gender

Gender	Pathology						
	Avascular necrosis N(%)	Osteoporosis N(%)	Metastasis N(%)	Bone cyst N(%)	Inflammatory reactions N(%)	Primary bone tumors N(%)	Total N(%)
Male	17 (70.8)	8 (53.3)	3 (33.3)	3 (60)	3 (42.9)	2 (50)	36 (56.3)
Female	7 (29.2)	7 (46.7)	6 (66.7)	2 (40)	4 (57.1)	2 (50)	28 (43.8)
Total	24 (100)	15 (100)	9 (100)	5 (100)	7 (100)	4 (100)	64 (100)

P-value =0.4, Fischer's exact test

DISCUSSION

With the increased prevalence of fractures, the prevalence of pathologic fractures is also increasing due to the growth in aging on the one hand and scientific and technological advances enabling the diagnosis and differentiation of this type of fracture from traumatic fractures on the other[7-9]. Pathologic fractures are found in bones already weakened by disease, tend to follow a minor trauma but may also occur without such incidences, and are associated with localized or generalized underlying diseases [1, 2]. In the present study, 56.3% of the patients were male and 43.8% were female. The mean age of the patients was 55.64±21.63. A total of 37.5% of the fractures were caused by avascular necrosis, comprising the most frequent pathology, while 6.3% were caused by primary bone tumors, comprising the least frequent pathology. The femur was the most frequent site of all the different types of pathologic fractures, which is consistent with the results obtained by other study that reported the most frequent site of fractures to be the femur, followed by the humerus[11]. In a study conducted by Maurer F and *et al.;* 57.3% of the fractures were caused by primary and secondary malignant tumors; however, the present study reported the most frequent underlying disease to be avascular necrosis, followed by senile osteoporosis and bone metastases [11]. Maurer's findings were not consistent with the results of the present study; however, they are in line with reference books.

Bonjour JP *et al.;* conducted a study in Switzerland and proposed osteoporosis as a frequent cause of pathologic fractures and claimed the risk of fractures caused by osteoporosis to be twice in women as in men and reported that 54% of women aged over 50 have experienced an osteoporotic fracture and that those aged over 60 will experience at least one more in their lifetime. The typical form of osteoporotic fractures affects vertebral bodies, the proximal femur and the forearm [12]. In a study conducted in the USA by Buckwalter JA, metastatic carcinomas were among the most frequent causes of pathologic fractures [13]. Davood pour conducted a study in 2003 to evaluate pathologic fractures in patients admitted to Shahid Mobasher Hospital of Hamadan, Iran, between 1991 and 1997 and found that pathologic fractures were more common in women (52.4%) than in men (47.6%). As for their frequency distribution, the highest frequency of pathologic fractures was observed in the 11-20 and 61-70 age groups. As for the etiology of the condition, senile osteoporosis was the most frequent cause of the fractures, and fibrous dysplasia, hyperparathyroidism and Paget's disease of bone were the least frequent causes, in respective order. The most frequent anatomical site of fractures in the cited study was the femur, and the least frequent sites were the pelvic bone and the metacarpal bone [14].The present study, however, did not show any significant relationships between gender and the frequency of fractures. Moreover, the 50-70 age groups was most frequently involved in pathologic fractures, and osteoporosis and primary and secondary bone tumors were the most common causes of getting fractures in the patients aged over 50.The results of the present study showed that the highest frequency of avascular necrosis causing pathologic fractures pertained to the 30-50 age group. Avascular necrosis (ischemic bone necrosis) is a bone disease caused by the temporary or permanent loss of blood supply to the bone and results in death and bone tissue collapse below the articular surface. The definitive diagnosis of necrosis can be made with a biopsy and different imaging techniques can be used for the diagnosis of avascular necrosis, including simple radiography, CT scan, bone scan and MRI, which vary significantly in terms of costs and diagnostic power [15]. Various studies have examined the factors affecting treatment outcomes in patients with femoral fractures and showed that, one year after the surgery, younger male patients with no underlying diseases such as diabetes show better outcomes than older female patients with underlying diseases and that the only cause of fractures in these patients is an avascular necrosis developed after a fracture [16,17]. Very few studies have examined patients with avascular necrosis and subsequent pathologic fractures, making the comparison of this finding with the findings of other studies impossible [18, 19].

Osteoporosis is the most prevalent disease that diffusively weakens the bones. Pathologic fractures caused by osteoporosis are found mostly in the lumbar vertebrae, the proximal femur and the wrist [2-10]. It should be noted that older people, especially older women, are more prone to osteoporosis. The risk of pathologic fractures is therefore higher in older people,

and when they occur, the bone lasts much longer to heal, thereby reducing the patients' daily physical activities and organic activities and affecting their nutritional status and potentially resulting in the further spread of osteoporosis if the patient is not treated in a timely manner. Different studies and statistics have shown that more than half of women aged over 45 and 90% of women aged over 75 show evidence of osteoporosis in their radiography [20, 21]. These individuals are at risk for factures and the risk factors associated with osteoporosis should be eliminated in them [20]. According to studies conducted on people with osteoporosis, fractures occur mostly in the bones that have a lower density and which are under higher pressure compared to the other parts of the skeletal system, such as the spinal cord. In the present study, the most frequent anatomical site of bone fracture after the femur was the spinal cord that is consistent with the results of other studies [19-21].

In a retrospective study conducted by Amin S et al. on 3549 people aged over 50 in Rochester, NY, between 2009 and 2011, the incidence of fractures increased with age in both genders; however, the average age of fractures was 49% higher in women. Avascular necrosis was the most frequent cause of pathologic fractures caused by a previous femoral fracture [22]. Although other studies also found underlying diseases to be associated with the incidence of osteoporosis, they gave a lower risk ratio to this factor than to some other risk factors (OR=2.853). The low prevalence of underlying diseases in the patients examined in the present study suggests the less importance of this factor. Studying the use of vitamin D and calcium supplements in patients with osteoporosis appears essential given that vitamin D and calcium are known as the main factors reducing the risk of pathologic fractures. It is also important to implement programs that improve people's knowledge of the role of these vitamins and minerals in the prevention of osteoporosis and subsequent pathologic fractures. These measures help reduce treatment costs and disease complications and achieve economic savings [23]. Malignant tumors such as multiple myeloma, lymphoma, and primary bone lesions such as, Paget's disease of bone and fibrous dysplasia can cause pathologic fractures, and bone tumors, whether malignant or benign, can weaken the bone and cause its fracture [1, 2, 4]. Metastatic tumors are the most frequent malignancies that locally weaken the bones and expose them to pathologic fractures. These tumors often involve the lumbar vertebrae and the proximal femur and humerus; however, almost no bone in the body is safe from these tumors. Primary and secondary tumors were the most frequent causes of pathologic fracture in the 50-70 age groups, while the femur was the most frequent bone involved in metastatic tumors. It therefore appears that this etiology should be more carefully considered in this age group [2, 3].The administration of vitamin D and calcium to women aged over 50 does reduce osteoporosis; however, given the increased prevalence of breast and lung cancer, metastatic bone involvement has also increased in this age group. In a study conducted in the US, by McDuffee LA *et al.;* concluded that most bone metastases occur in cases of breast, prostate, lung and kidney cancer, that 30%-70% of patients with cancer suffer from bone metastasis and that bone metastasis is the third site of metastasis after the lung and the liver [24]. The researchers argued that metastasis to the spinal cord comprise half of bone metastases and is followed by femoral and humeral metastases. They also reported breast cancer to be the main cause of pathologic fractures [24]. Simple bone cysts are also frequent causes of pathologic fractures, as they were observed even in the patients fewer than 30 examined in the present study, which is consistent with the findings of other studies [25].

The low number of pathologic fractures referred to the pathology department of the select hospital comprises an interesting finding of the present study, which could be due to how a lot of pathologic fractures are either suboptimal and present with few symptoms, resulting in the patients' failure to seek care, or how they are micro fractures diagnosed by radiology and treated non-surgically.

CONCLUSION

The findings of the study showed a high prevalence of pathologic fractures in patients with avascular necrosis and osteoporosis, given that the most frequent cause of pathologic fractures was avascular necrosis in younger and osteoporosis in older patients. Since a case of fracture may be followed by avascular necrosis, early medical interventions should be taken to prevent this condition and reduce its subsequent complications, such as pathologic fractures, in patients suffering from a fracture. The incidence of osteoporosis and subsequent fractures should also be reduced through the administration of vitamin D and calcium to older people. Primary and metastatic tumors should be regarded as the main etiology of pathologic fractures in the 50-70 age groups.

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