

Prevalence and risk factors for pathological fracture among end stage renal disease patients

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Abstract

Background: Pathological fracture diagnosis is on rise. The morbidity involved doesn't only load the patients and their families but it has a great cost on the health care system as well.

Aims of the Study were to estimate the prevalence and assess risk factors for pathological fracture among patents with end stage renal disease.

Patients and Methods: Overall, 500 patients on maintenance hemodialysis (HD) were included in a descriptive cross-sectional study. The study was conducted at Assiut University Hospitals (Assiut – Egypt). Data pertinent to the study was collected by utilizing the following tool: Patients' structured interview assessment sheet: it included two parts: Part one: sociodemographic data. Part two: clinical assessment data.

Results: 6.8% of the studied sample had exposed to pathological fracture where the hip, radius/ ulna, and vertebra were the most common sites affected. In univariate logistic regression; it was found that six factors had significant predicted relations with pathological fracture (duration of hemodialysis, overweight, coronary artery diseases, radiation exposure, parathyroidectomy, and pancreatic diseases) while in multivariate logistic regression; it was found that three factors (duration of hemodialysis, radiation exposure, and parathyroidectomy) were significant as in univariate logistic regression plus four factors (age, sex, diabetes, and hypertension) which were significant too.

Conclusion: In our study the prevalence of pathological fracture among end stage renal disease patients occurred by 6.8% and there was significant relation between pathological fracture & ten risk factors.

Recommendations: Early identification of the patients who are at risk for pathological fracture is a valuable tool to cut cost and improve patients' quality of life.

Keywords: prevalence, risk factors, pathological fracture, end stage renal disease

Introduction

Pathological fracture is a break in the continuity of bone that is caused by a disease, rather than an injury. By nature, it occurs through bone that is biologically abnormal and where the response to and potential for healing can be dramatically different from normal bone for a variety of reasons. Fracture that occurs among end stage renal disease (ESRD) patients often is a deterioration that accompanies chronic kidney disease (CKD) as it progresses (Leslie & Lix, 2014) [17].

Chronic kidney diseases defined as abnormalities of kidney structure or function, presents for ≥ 3 months with implication for health. Based on kidney function, i.e. glomerular filtration rate (GFR), CKD is classified into five stages: stage 1: GFR > 90 ml/ min, stage 2: GFR 60-89 ml/min, stage 3: GFR 30-59 ml/min, stage 4: GFR 15-29 ml/min and stage 5: GFR ≤ 15 ml/min. Stage 5; represents kidney failure or end stage renal failure (Miller, 2014) [18].

It must be kept in mind that end stage renal failure differ from kidney failure, (ESRD) includes all patients treated by dialysis or transplantation irrespective of the level of GFR. While kidney or renal failure is defined as either (1) a level of GFR to < 15 ml/ min. which is accompanied in most

cases by signs & symptoms of uremia. Or (2) a need for initiation of renal replacement therapy (National Kidney Foundation, 2016) [20].

Renal replacement therapy includes renal transplantation or dialysis, the later replaces non endocrine kidney function in patients with renal failure. All dialysis modalities exchange solute & remove fluid from the blood using dialysis and filtration across permeable membranes. RRT doesn't correct the endocrine abnormalities (decreased erythropoietin, 1.25 dihydroxy vitamin D3 productions) of renal failure which in turn lead to mineral and bone disorders and renal osteodystrophy (Jamal *et al.*, 2012) [14].

Mineral and bone disorders develops as a systemic disorders of mineral and bone metabolism caused by progressive deterioration in kidney function. As kidney function deteriorates, less vitamin D is converted to its active form, resulting in decreased serum levels. Activated vitamin D is necessary to optimize absorption of calcium from the GI tract; thus low levels of active vitamin D result in decreased serum calcium levels. PTH is the primary regulator of serum calcium levels. When hypocalcaemia occurs (Brancaccio & Cozzolino, 2011) [6].

The PTH acts on the bone which results in the high-turnover bone disease. In addition, a different skeletal abnormality known as adynamic bone, which is characterized by an extremely low bone turnover, may occur. Some cases may demonstrate mineralization defects and show frank osteomalacia. This wide spectrum of skeletal abnormalities can give rise to a variety of mixed patterns, with elements of the effects of hyperparathyroidism on bone together with mineralization defects, and is known as mixed renal osteodystrophy which places the patient at a higher risk for fractures (Hans *et al.*, 2011) [12].

Pathological fracture among hemodialysis patients is complicated & likely is multifactorial. Some fractures have been associated with low vitamin D, low parathyroid hormone levels, and low bone mass, osteoporosis, poor nutrition, inactivity, myopathy, and peripheral neuropathy which increase the risk of falling and lead to fracture. (Garcia *et al.*, 2014) [9]

Early recognition of risk factors is the most important components of nursing care. Teaching patients to take appropriate safety precautions to prevent injuries, encourage them to participate in moderate exercise to help maintain muscle strength and balance. To reduce falls, they should wear adequate footwear and assess their living environment for safety, stress the importance of adequate calcium and vitamin D intake. (Patrice, *et al.*, 2011) [21]

Significance of the study

Although bone disease is well described among end-stage renal disease (ESRD) patients, little attention has been paid to the occurrence of fracture. It is one of the biggest causes of morbidity in patients undergoing dialysis; it has high mortality rate, decreased quality of life, and large economic burden. Hence this study was carried out to estimate the prevalence and assess risk factors for pathological fracture among our studied patients.

Aims of the study

- To estimate the prevalence of pathological fracture among patients with end-stage renal disease.
- To assess risk factors for pathological fracture among patients with end-stage renal disease.

Research questions

1. What is the prevalence of pathological fracture among patients with end-stage renal disease?
2. What are the risk factors for pathological fracture among patients with end-stage renal disease?

Patients and Methods

Research design

A descriptive cross-sectional research design was utilized to fulfill the aims of this study.

Setting

The study was conducted at Dialysis unit, Om El- Kosor hospital of Assiut University Hospital, & El- Azhar University Hospital.

Sample

Overall, 500 patients, 202 females and 298 males, on

maintenance hemodialysis (HD) were included in a cross-sectional study after obtaining their informed consent. The mean age was 56.4 ± 12.4 years and the mean duration of HD treatment was 5.7 ± 3.727 (0.5-18) years. All of the patients were on bicarbonate dialysis with a calcium concentration of 135 mmol/L for 12–15 hours per week for the last 5 years with hollow-fiber dialyzers with a polysulfone membrane (fiber glass). Blood flow was 200–300 mL/min, and the flow of the dialysate was 500 mL/min. The water for dialysis was prepared by the reverse osmosis method. Its conductivity was below $10 \mu\text{s}/\text{cm}^3$ and temperature was 37°C . All of the patients in therapy had been treated with (Calcimax, Ribagel) according to the clinical recommendations for patients being treated by HD. Patients were not treated with estrogens and calcitonin. Psychiatric conditions were excluded.

Tool

Patient structured interview assessment sheet:

This sheet was prepared by the researchers based on national & international literatures review to assess patients' sociodemographic data, and clinical assessment data. It included two parts:

Part I: Socio-demographic data

This part assessed socio-demographic characteristics of studied patients (e.g., age, sex, residence, marital status, levels of education, and occupation).

Part II: Clinical assessment data

This part included detailed information as duration of receiving hemodialysis, body mass index, comorbid conditions, history of previous or current fracture, sites, and mechanism of injury.

Methods

Ethical approval for human rights

An official permission to conduct the study was obtained by the researchers from the chief of the above mentioned settings. At initial interview, each patient was informed with the purposes of the study. The investigator emphasized that the participant is voluntary and confidentially and anonymity of subjects will be assured through coding of all data.

Pilot Study

The purpose of pilot study was two folds: first to ensure the clarity of designated study tools. Second, to examine the utility of the designed tools and identify any difficulties or problems needed to be handled before applying it. Those patients who were involved in the pilot study were excluded from the actual study sample. Modification of the sheet was done to develop the final form for data collection.

Content Validity

It was established by a panel of five expertise (Medical Surgical Nursing, & Medical "Nephrology" fields). who reviewed the instruments for clarity, relevance, comprehensiveness, understanding, applicability, and easiness for administration. Minor modifications were required.

Procedure

Once permission was granted to proceed with the proposed study, the investigators initiated data collection. Names of patients who are admitted to Kidney Dialysis Unit were obtained from them to accomplish this research work. As well as a non-official permission from the patients was obtained. Structured interview was utilized to fill out the structured interview assessment sheet (tool 1). There was exactly detectable length of time in the interview, because patients are attending to the unit 3 times per week (Saturday, Monday, and Wednesday), other patients (Sunday, Tuesday, and Thursday). These patients are divided into sessions according to the policy of the hemodialysis units i.e. first session, second session, third session, and fourth session, each session involved about 50 patients. The researchers were visiting the units twice a week; Mondays and Thursdays in each session every week until the assessment process was completed. The number of patients in this study whose fracture diagnosis was based on imaging was unknown, clinical diagnosis was based on either previously or currently occurrence of fracture.

Data analysis

The data were tested for normality using the Anderson-Darling test and for homogeneity variances prior to further statistical analysis. Categorical variables were described by number and percent, while continuous variables described by mean and standard deviation. Univariate logistic regression analysis was used to assess age, sex, and patients' comorbidities as risk factors for pathological fracture then multivariate logistic regression analysis was conducted. P value less than 0.05 was considered statistically significant. Odds ratios and 95% confidence intervals (CIs) were calculated. All analyses were performed with the IBM SPSS 20.0 software.

Limitation of the Study

1. Lack of financial support to do laboratory investigations (dual-energy X-ray absorptiometry (DEXA), parathyroid hormones (PTH), Calcitonin, serum calcium, and vitamin D, ect....) for all patients which can help in accurate estimation of all risk factors.
2. The sample size was limited in generalizability because the sample was selected from one geographical area in Arab Republic of Egypt.

Analysis of the result:

Table 1: Percentage distribution of socio demographic characteristics of ESRD patients (n = 500).

Socio demographic characteristics	No	%
Age	92	
18- <34 years	176	18.4
34< 49 years	232	35.2
50≤ 65 years		46.4
Mean ±SD (Range)	46.9±12.4(18-65)	
Sex		
Male	298	59.6
Female	202	40.4
Residence		
Rural	366	73.2
Urban	134	26.8
Marital status		
Single	59	11.8
Married	422	84.4
Divorced	10	2.0
widow/widew	9	1.8
Educational Level		
Illiterate	206	41.2
Read and write	79	15.8
preparatory	16	3.2
Secondary	158	31.6
University	41	8.2
Occupation		
Office work	77	15.4
Machinery work	28	5.6
Farmer	127	25.4
House wife	172	34.4
Retired	36	7.2
Student	12	2.4
Not working	48	9.6

Table 2: Frequency distribution of pathological fracture among ESRD patients (n= 500).

Pathological fracture	No	%
Pathological fracture		
- Yes	34	6.8
- No	466	93.2
If yes; fracture site		
- Radius &/or ulna	10	29.4
- Hip	15	44.11
- Vertebra	9	26.47
- Forearm	0	0.0
Mechanism of injury		
- Road traffic accident(RTA)	4	11.76
- Fall from high	10	29.4
- Fall on ground	20	58.82

Table 3: Percentage distribution of clinical assessment data among ESRD patients (n = 500).

Clinical assessment data	No	%
Duration of receiving hemodialysis		
<5	52	10.4
5-10	175	35.0
>10	273	54.6
Mean ±SD (Range)	5.7±3.727(0.5-18)	
BMI		
Underweight	12	2.4
Normal	154	30.8
Overweight	111	22.2
Obesity	223	44.6

Diabetes mellitus		
Yes	200	40.0
No	300	60.0
If yes		
Controlled	150	30.0
Uncontrolled	50	10.0
Hypertension		
Yes	396	79.2
No	104	20.8
If yes		
Controlled	135	27.0
Uncontrolled	261	52.2
Coronary artery diseases		
Yes	116	23.2
No	389	76.8
Radiation therapy exposure		
Yes	16	3.2
No	484	96.8
Parathyroidectomy		
Yes	34	6.8
No	466	93.2
Pancreatic diseases		
Yes	20	4.0
No	480	96.0

BMI: body mass index

Table 4: Binary logistic regression analysis for prediction of pathological fracture risk factors among end stage renal disease patients.

Predictors	Univariate logistic regression			Multivariate logistic regression		
	Odd ratio	95% CI	P. value	Odd ratio	95% CI	P. value
Age	0.976	0.95 – 1	0.068	0.948	0.91 - 0.99	0.018*
Sex (Male) ref.	0.509	0.23 - 1.12	0.092	3.815	1.1 - 13.21	0.034*
Duration	1.364	1.25 - 1.49	<0.001**	1.458	1.25 - 1.71	<0.001**
Body mass index (Underweight) ref. Normal	4.26	0.82 - 22.08	0.084	7.972	0.6 - 106.2	0.116
Overweight	2.643	1.18 - 5.94	.019*	1.544	0.49 - 4.86	0.458
Obesity	1.005	0.34 - 3.01	0.993	1.393	0.3 - 6.47	0.672
Diabetes	0.647	0.32 - 1.3	0.221	0.149	0.04 - 0.54	0.004**
Hypertension	1.186	0.52 - 2.7	0.685	7.159	1.89 - 27.14	0.004**
Coronary artery diseases	0.351	1.72 - 0.71	0.004**	0.419	0.12 - 1.5	0.182
Radiation exposure	0.102	0.04 - 0.3	<0.001**	39.604	1.07 - 1467.69	0.046 *
Parathyroidectomy	0.064	0.03 - 0.15	<0.001**	0.047	0.01 - 0.19	<0.001**
Pancreatic diseases	0.067	0.03 - 0.18	<0.001**	0.163	0.02 - 1.46	0.105

Dependent variable is the fracture, CI: Confidence interval, *0.01<P≤0.05; **P<0.01.

Table (1): shows 500 patients on maintenance hemodialysis. The highest percentage of age (46.4%) was regarding to patients that their age ranged from 50 ≤ 65 yrs than other groups, with a mean age of (46.9±12.4). Also the highest percentage of patients were male, married, and illiterate (59.6%, 84.4%, & 41.2% respectively). Also it was found from the same table that 34.4% of patients were house wives & 25.4% were farmers. Majority of patients (73.2%) came from rural while only (26.8%) of patients came from urban. Table (2) reflects that; 6.8% had exposed to fracture where the hip, radius/ ulna, and vertebra were the most common sites affected.

Table (3) reflects that; more than half of studied patients were receiving haemodialysis for more than ten years. Also it was found from the same table that 200 patients had diabetes; 150 of whom were controlled and 50 patients uncontrolled. 396 patients had hypertension; 135 of whom were controlled & 261 patients uncontrolled. About one fifth (23.2%) of studied patients had coronary artery disease. A few number of patients had pancreatic diseases, exposed to radiation therapy, and had undergone parathyroidectomy

(4.0%, 3.2%, and 6.8% respectively)

Table (4) demonstrates regression analysis for ten risk factors; in univariate logistic regression; it was found that six factors had significant predicted relations with pathological fracture (Duration of HD, Overweight, coronary artery disease, Radiation exposure, Parathyroidectomy, and Pancreatic disease) as the odd ratio were (1.364, 2.643, 0.351, 0.102, 0.064, & 0.067 respectively) while in multivariate logistic regression; it was found that three factors (duration, radiation exposure, and parathyroidectomy) were significant as in univariate logistic regression plus four factors (age, sex, diabetes, and hypertension) as the odd ratio was (0.948, 3.815, 0.149, & 7.159 respect.) which were significant too.

Discussion

To our knowledge; no nursing studies have been carried out on this topic. Ultimately by estimation of the prevalence and assessing risk factors for pathological fracture among hemodialysis patients and targeting those patients will reduce the risk of fracture among this group of patients. A

total of five hundred adult patients on maintenance hemodialysis were studied.

In relation to their sociodemographic data, the results of the present study demonstrated that, more than half of studied patients have an age ranged from 50-65 yrs old. This finding was supported by (John *et al.*, 2014) [15] who found in their study that most of the increase in fracture rate segregated to white patients that their age between 50 and 60 years, with greater incidence in women than men. This was on the contrary with the result of the present study which pointed that more than half of the studied patients were males. Regarding marital status, the findings of this study indicated that less than two third of patients were married. Similar finding was revealed by (Ali, 2014) [2], found that the majority of patients were married. On the other hand, Ayub (2014) [3] revealed contradictory results, where the majority of patients were single and divorced because kidney disease affected on their sexual life.

According to the prevalence of pathological fracture among our studied patients; it was found that thirty four patients had exposed to fracture. This could be attributed to renal osteodystrophies that accompanies CKD & dialysis process which in turn may lead to low bone strength, decreased overall physical capabilities and increases the risk of falls leading to fracture. This study finding is inconsistent with the study of (Iva Šimunović *et al.*, 2015) [13] who reported that the prevalence of patients with bone fractures was 4.0%.

According to fracture site, the results of the current study illustrated that the hip, radius/ ulna, and vertebra were the most common sites affected. This study finding was supported by (Link, 2012) who reported that spine, hips, and forearms are the most common sites of fractures resulting from osteoporosis in hemodialysis patients. Additionally, (Mittalhenkle *et al.*, 2004) [19] observed in their study that hip fractures are seen approximately twice in patients with end stage renal disease as often as in patients without CKD and the risk of fracture is increased in patients who have had longer exposure to dialysis and this is consistent with our study findings as there was significant relation with the duration of hemodialysis and fracture among end stage renal disease patients.

To examine the risk factors for the increasing pathological fracture in hemodialysis patients. Specific demographic characteristics were studied. Old age and male sex were independent predictors for pathological fracture in our study. This finding is consistent with prior study by (Ball *et al.*, 2002) [5] which has shown that demographic characteristics including increasing age, and female sex were associated with an increased risk of hip fracture. But our study did not identify female gender as an independent risk factor for pathological fracture in ESRD patients. This may be attributed to increase number of male patients in the studied sample.

This study has confirmed that there were many risk factors have a significant relations and independent risk factors for fracture that result from either one or the combination of these conditions. If we looked for the association between diabetes and fracture among our studied patients it may be due to many reasons that involve inadequate glycemic control, greater risk of falling as a consequence of hypoglycemia, osteopenia, impairment of bone quality, and

side effects of medication, which could lead to a higher risk of bone fragility and fractures.

Additionally (Abdallah, 2010) [1] reported that DM and HTN are the number 1 and 2 conditions, respectively, that lead to chronic kidney disease. Hence, most patients with ESRF also have DM and HTN. This too is consistent with the findings of this article which revealed that; 200 patients with ESRF in our study had diabetes; 150 of whom were controlled and 50 patients uncontrolled. 396 patients had hypertension; 135 of whom were controlled & 261 patients uncontrolled.

With regard to the association between parathyroidectomy and pathological fracture in our data, it was found that there was a significant relation between parathyroidectomy and pathological fracture, It may be attributed to most patients often require parathyroidectomy as a definitive treatment when a pathologic fracture occurs due to increase secretion of parathyroid hormone which increase bone resorption, causes high bone turn over, and reduced bone mineral density predisposing to pathological fractures. This was consistent with (Rudser *et al.*, 2007) [22], as they found that fracture risk is lower in parathyroidectomy patients. On the other hand, (Coco *et al.*, 2000) [7] identified a higher risk of fracture in patients with low serum PTH level.

According to the association between body mass index and pathological fracture in the current study, it was found that there was a significant relation between overweight and pathological fracture, this is contrast with (De Laet *et al.*, 2005) [8] who reported that elevated bodyweight is positively correlated with increased bone mineral density and with reduced risk of fragility fractures. Our data are also inconsistent with a report of (Kajala *et al.*, 2000) [16] who found that the risk of hip fracture decreased by 12% (95% CI 3 to 20%) for each unit increase in BMI. In the researchers' point of view, BMI may be a marker for an underlying illness that increases the risk of fracture. Alternatively a higher BMI may independently influence the characteristics of bone by increasing the mass of adipose tissue available for estrogen production or increasing the padding at the hips to decrease the forces during a fall.

As regard to the association between duration of receiving hemodialysis and pathological fracture in the present study, it was found that there was a significant relation between duration of receiving hemodialysis and pathological fracture. This finding was similar with (Iva Šimunović *et al.*, 2015) [13] who mentioned that fractures were more often observed in patients on hemodialysis for more than five years and the risk of fracture is increased with longer period of haemodialysis.

Also the results of the present study showed a significant relation between coronary artery diseases and pathological fracture. Most patients with ESRD had coronary artery diseases, this could be explained by structural and functional abnormalities of the vasculature that can be seen in early CKD, including vascular stiffness and endothelial dysfunction that progress to vascular calcification. Furthermore, it was reported by (Go *et al.*, 2004) [11] that patients with ESRF, had a higher prevalence of coronary heart disease, stroke or transient ischemic attack, peripheral arterial disease, and chronic heart failure. Regarding the association between pancreatic disease and pathological fracture in the present study, it was a

significant relation between pancreatic disease and pathological fracture. This is consistent with (Baba *et al.*, 2011) [4], who found that there were very few cases of vertebral fracture induced by pancreatitis.

There was a significant relation between radiation exposure and pathological fracture. This is consistent with prior study achieved by (Sternheim *et al.*, 2013) [23] which revealed that there were 697 patients with a soft-tissue sarcoma of the hip and thigh who had been treated by resection with adjuvant radiotherapy. A radiation-induced fracture of the femur occurred in 31 patients (4.4%) after management.

Conclusion

We present the study results to the larger community; which may have additional supportive data or the means to effectively answer the study questions. In our study, ESRD was associated with a pathological fracture. There were significant relations between pathological fracture & ten risk factors (Duration, overweight, coronary artery disease, radiation therapy, parathyroidectomy, pancreatic disease, age, sex, diabetes, and hypertension).

Recommendations

For patients

- Early identification of the patients who are at risk for pathological fracture is invaluable tool to cut cost and improve patients' quality of life.
- A fall prevention program for patients who are at risk would be of paramount importance.

In services

- Proper screening for the early detection of pathological fracture in ESRD patients to reduce the burden of morbidity and mortality in this subset of patients.
- For further studies and research
- Further studies would be beneficial as many occult problems in hemodialysis patients remain unclear.
- Replication of the study using a larger probability sample acquired from different geographical areas.

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