

## THE PREVALENCE OF RADIOLOGICAL MARKERS OF RENAL OSTEODYSTROPHY IN PATIENTS WITH CHRONIC RENAL FAILURE IN ENUGU.

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### ABSTRACT

**Objectives:** To study the prevalence of renal osteodystrophy in Chronic renal failure patients in Enugu, using radiological methods.

**Subjects and Methods:** Ninety adult patients (56 male and 34 female) were recruited from the renal clinics of the University of Nigeria Teaching Hospital, Enugu over a period of twelve consecutive months.

A structured questionnaire was administered and a physical examination carried out at the initial interview. This was followed by other investigations including renal ultrasonography, plain radiographs and laboratory investigations including serum electrolytes, urea and creatinine, calcium and phosphate, total alkaline phosphate and creatinine clearance estimation.

**Results:** There was no obvious relationship between bone pain (a symptom of renal osteodystrophy) and the presence of radiological features of renal osteodystrophy.

The findings of the study showed that renal osteodystrophy, demonstrable by radiography is relatively uncommon, existing in only 3 subjects (3.35%). Among the 3 subjects, 2 showed radiological features of osteitis fibrosa cystica (one male and one female), while the other subject (one female) had radiological features of osteoporosis. All these subjects belonged to group 3 and had been on maintenance haemodialysis for more than 6 months.

Other forms of renal osteodystrophy were not demonstrated.

**Conclusion:** Renal osteodystrophy is probably not as common in Nigerian patients as in Caucasians and there may be reasons for this.

**Key words:** Glomerular filtration rate, renal disease, dialysis.

### INTRODUCTION

Renal osteodystrophy embodies a group of bone changes noted in patients with advanced Chronic renal failure. These include- Osteitis fibrosa cystica, Osteosclerosis, adynamic bone disease and mixed forms. In children, rickets, skeletal deformities and growth retardation may be present. Osteitis fibrosa cystica and osteosclerosis are high bone turnover states due to secondary hyperparathyroidism, while osteomalacia and osteoporosis are low bone turnover states. In osteomalacia, there is increased volume of osteoid (unmineralised bone). Adynamic bone disease is a relatively new form of low bone turnover state which has been increasing in prevalence since the last ten years. The volume of osteoid in this condition is not increased. With radioimmunoassay techniques, high parathyroid hormone levels are detected in early stages of Chronic renal failure.

Several factors contribute to the development of hyperparathyroidism. These include Hypocalcemia, hyperphosphatemia, decreased vitamin D synthesis and resistance to its action, decreased calcemic response to parathyroid hormone degradation among others<sup>1</sup>. These factors have a synergistic effect on each other and altered parathyroid hormone and so combine to produce the clinical effects noted at any particular time. When these factors are sustained, hyperparathyroidism becomes maladaptive, producing bone disease and contributing to the dysfunction in other organs. With modern and better management of patients with end stage renal disease, especially with the advent of renal replacement therapy, resulting in increased life span for Chronic renal failure patients, the prevalence, distribution and course of these bone abnormalities have markedly changed. Symptoms due to these disorders such as fractures and bone pain, generally do not occur until the patient is already on maintenance dialysis<sup>2</sup>.

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Less than 10% of patients with Chronic renal failure manifest with clinical features of renal osteodystrophy before dialysis, but 35% of patients with advanced Chronic renal failure show radiological evidence of renal osteodystrophy<sup>3</sup>. Though histology is more sensitive than radiology in diagnosis of renal osteodystrophy, histological methods are more cumbersome and invasive, and require a histopathologist experienced in this field. These features are difficult to overcome in Nigeria at this time. The pattern of renal osteodystrophy has been shown to differ from region to region. Studies in Asians showed more mild forms of aluminium related bone disease<sup>4</sup>. Black patients with end stage renal disease have a greater bone mineral density and are at decreased risk of osteopenia compared with whites, independent of renal osteodystrophy<sup>5</sup>. There may also be a tendency to gender bias, with women seemingly at high risk for development of hyperparathyroidism, whereas aplastic bone disease may be related to the male gender in patients undergoing chronic ambulatory peritoneal dialysis<sup>6</sup>. In Nigeria, it is generally believed that renal osteodystrophy is rare probably because our end stage renal disease patients do not live long enough for this disorder to manifest<sup>7</sup>. However, with the growing availability of renal replacement therapy in the country and so better management and longer life for end stage renal disease patients in the last decade, this belief may no longer be tenable. This study is a cross sectional, descriptive study to find the prevalence of renal osteodystrophy (using radiological methods) in chronic renal failure patients in Enugu, which is a metropolitan Nigerian city with a teaching hospital and a well established renal unit.

## MATERIALS AND METHODS

**1.1 Patient selection** The study was carried out between March 2001 and March 2002, at the University of Nigeria Teaching Hospital, Enugu, which is a 760 bed tertiary hospital with a well developed renal unit. It draws its patient population from all over Nigeria, however majority of patients come from neighboring south eastern and south southern parts of the country. The study was approved by the ethical committee of the institution. The subjects were drawn from consecutive chronic renal failure patients attending the renal clinics of the University of Nigeria Teaching Hospital, Enugu, who met the following criteria: Adults of eighteen years and above, who had a glomerular filtration rate of 20mls/min and below and who did not have sickle cell disease, liver disease, evidence of primary or metastatic bone disease or diabetes mellitus. Informed consent was obtained from these patients.

**1.2 Study design** Those who satisfied the above conditions were required to complete a researcher administered questionnaire detailing among other things, biodata, symptoms and their duration, medications, usual diet, duration and frequency of dialysis, concomitant illnesses like diabetes mellitus, sickle cell disease and others. A general examination was carried out. Ten milliliters of venous blood was drawn from a suitable vein and collected in a clean plain blood container with minimal stasis and used to assess serum creatinine, calcium, phosphate, alkaline phosphatase, gamma glutaryl transpeptidase and albumin levels. Glomerular filtration rate was determined by 24-hour urine creatinine clearance. Plain X-ray of the phalanges of hands, pelvis, lower spine and skull were carried out and reported by an experienced consultant radiologist under magnification. Ultrasound of the kidneys was carried out to establish chronic renal failure.

**1.3 Technique** The radiographs were taken by experienced radiographers, using a standard X ray machine with good resolution qualities.

(a) Hands

The patient was placed in postero-anterior position, with the forearm placed on the table in pronation, with the fingers extended, but relaxed and separated to bring them in close contact with the film. The beam center was over the head of the third metatarsal bone. The factors were 60kv and 3 MAS focus. Film distance was 90cm. The film was read under magnification by a consultant radiologist.

(b) Pelvis

The view is Anteroposterior. Patient position is supine. Both legs internally rotated 15° to 20°. Beam is centered mid sagittal plane mid way between symphysis pubis and iliac crest. Ray should be perpendicular to film holder.

(c) Lumbar spine

The views are Anteroposterior and Lateral.

Anteroposterior - Patient position is supine with hips and knees flexed and head on pillow. Center to the level of iliac crest (L<sub>4</sub> L<sub>5</sub>), perpendicular to the film holder. FFD = 102cm.

Lateral Patient position is lateral recumbent usually left center to iliac crest, perpendicular to film holder. FFD = 102cm.

## RADIOLOGIC FEATURES

1. Features of Hyperparathyroidism

- (a) A principal feature is bone resorption and erosions which may occur on the subperiosteal, intracortical and endosteal surfaces of cortical bone.
- (b) Periosteal neostosis which is the presence of new Bone formation at the periosteal surface.

- (c) Osteopenia and osteosclerosis.
- (d) Intracortical striations
- (e) Cysts or osteoclastomas (brown tumors).
- (f) 'Rugger jersey' appearance of vertebrae signifying patchy osteosclerosis.
- (g) Salt and pepper appearance of skull.

## 2. Features of Osteomalacia

- (a) Loosers zones or pseudofractures
- (b) True fractures
- (c) Compression fractures of the vertebral bodies
- (d) Protrusio acetabuli convex bulging into the pelvis over the acetabulum.
- (e) Skeletal demineralization
- (f) Increased haziness or coarsening of the Trabeculae.
- (g) Biconcavity of the vertebral bodies (especially in association with normal bone density).
- (h) Bending deformities of long bones.

## 3. Features of Osteopenia or Osteoporosis

- (a) Periarticular rarefaction.
- (b) Loss of trabecular bone with a honey comb or fishnet pattern.
- (c) Loss of cortical bone from the endosteal surface

## 4. Extraskkeletal Calcifications

- (a) Calcification of medium sized arteries.
- (b) Periarticular calcifications
- (c) Visceral calcifications, which can involve the heart, lung and kidney.  
(Brenner and Rector's; The Kidney vol. 25<sup>th</sup> edition 1999)

## RESULTS

**3.1 Patient Demographics** - Between March 2001 and March 2002, a total of 316 patients attending the renal clinics dialysis unit of the University of Nigeria Teaching Hospital, Enugu, were screened for the study. Ninety of them were selected, having met the inclusion criteria. The study population included 56 males and 34 females. Their ages ranged from 18 to 65 years (see table below).

Table 1 shows the age and sex distribution of the subjects in this study. A total of ninety (90) subjects were enrolled with age range of 16-65 years. Mean age for males 38.6811.44 years and for females 37.4710.98 years. The mean age for the general study population (male and female) is 38.22 11.22 years.

**3.2 Duration of uremic symptoms** The patients were grouped into 2 based on duration of symptoms of chronic renal failure

- Those with duration of symptoms < 6 months
- Those with duration of symptoms > 6 months.

Among the subgroup with duration of symptoms > 6 months, a total of 2 patients (one male and one female) had radiological features of osteitis fibrosa cystica. Another female subject in the same subgroup with duration of symptoms > 6 months had radiological features of osteoporosis.

**3.3 Correlation between bone pain and radiological features** - Six males and five females in this study had bone pain. All of them had radiological features of osteoarthritis in affected bones. 17 subjects (8 males and 9 females) showed radiological evidence of osteoarthritis, but had no bone pain. All the patients with radiological evidence of renal osteodystrophy (2 females and one male) had no symptom of bone pain.

## 3.4 Distribution of patients on haemodialysis.

None of the patients in group one (glomerular filtration rate 11- 20mls/min) was on maintenance dialysis.

In group 2 (glomerular filtration rate 6-10mls/min), 9 males and 5 females had been on maintenance haemodialysis for less than 6 months. Only 2 male subjects and no female subject had been on dialysis for more than 6 months.

In group 3 (glomerular filtration rate 5mls and less), all the subjects were on maintenance haemodialysis. 20 male and 12 female subjects had been on maintenance haemodialysis for less than 6 months, while 10 male and 10 female subjects had been on maintenance haemodialysis for more than 6 months (see table 2).

All the subjects with renal osteodystrophy (2 females and one male) were in group 3 and had been on maintenance haemodialysis for more than 6 months.

**3.5 Type of renal osteodystrophy seen in the subjects** - 3 subjects out of 90 (3.35%), showed radiological evidence of renal osteodystrophy. Two of them (one male and one female), showed radiological features of osteitis fibrosa cystica, while one female patient showed radiological features of osteoporosis.

**Table 1: Age and Sex Distribution of Patients.**

Age (yrs)	Number		
	Male	Female	Total
16 – 25	8	4	12
26 – 35	17	13	30
36 – 45	14	11	25
46 – 55	14	3	17
56 – 65	3	3	6
<b>Total</b>	<b>56</b>	<b>34</b>	<b>90</b>
<b>Mean Age</b>	<b>38.68 yrs</b>	<b>37.47 yrs</b>	<b>38.22 yrs</b>
<b>± SD</b>	<b>± 11.44 yrs</b>	<b>± 10.98 yrs</b>	<b>± 11.22 yrs</b>

**Table 2: Distribution and Duration of Patients on Haemodialysis.**

Duration on aemodialysis	Group I n = 13		Group II n = 25		Group III n = 52	
	M	F	M	F	M	F
Not on Haemodialysis	9	4	6	3	-	-
< 6 months	-	-	9	5	20	12
> 6 months	-	-	2	-	10	10
<b>Total</b>	<b>9</b>	<b>4</b>	<b>17</b>	<b>8</b>	<b>30</b>	<b>22</b>

**DISCUSSION**

The principal findings of this study suggest the following

- Renal osteodystrophy demonstrable by radiological methods is uncommon in Nigerian chronic renal failure patients.
- Osteitis fibrosa cystica is the commonest type seen.
- Radiological evidence of renal osteodystrophy appears to be more prevalent in those with longer duration of chronic renal failure.
- There is no correlation between bone pain and radiological features of renal osteodystrophy.
- Renal osteodystrophy may be more prevalent in females.

**4.1- Prevalence of radiological renal osteodystrophy.** Radiological evidence of renal osteodystrophy was found in only 3 out of the 90 patients studied (3.35%). Two of these were female patients out of a total of 34 females enrolled in the study (5.58%), while one was male, out of a total of 56 males (1.8%) studied. All the subjects found with renal osteodystrophy belonged to group 3 (glomerular filtration rate ≤ 5mls/min).

This finding is much lower than that reported from studies from western countries. Shin-s k et al, found an incidence of 91.4% in chronic renal failure patients before commencement of dialysis in Canada<sup>4</sup>. Their study was however based on bone biopsy results, which are known to be more sensitive than radiological methods. Hodson et al, reporting from Germany, found that out of 17 patients with renal osteodystrophy, only 7 had radiological evidence of renal osteodystrophy, while all 17 patients were positive by bone biopsy<sup>6</sup>. This may in part explain the disparity between our result and that of other studies. Owen J P et al, found disappointing levels of agreement between different radiologists in England, in interpretation of radiographs of renal osteodystrophy<sup>7</sup>. This may be due to the use of different techniques and level of expertise. Stehman-Breen-co et al, found that black patients with end stage renal disease in the U.S.A., have a greater bone mineral density and are at decreased risk of osteopenia, compared with whites independent of renal osteodystrophy<sup>5</sup>.

Most of the patients in our study had a relatively short duration of symptoms (55.6% had duration below 6 months), this may in part explain the low prevalence of radiological findings, since radiological features of renal osteodystrophy tend to occur late. Also radiology clearly reflects only the cortical bone and not the cancellous bone, so some types of renal osteodystrophy may not be readily evident radiographically.

**4.2- Osteitis fibrosa cystica is the commonest type detected** - 3 subjects out of 90, showed radiological features of renal osteodystrophy. Two of these (66.7%), one male and one female, had radiological features of osteitis fibrosa cystica. The third subject (33.3%), a female, had radiological features of osteoporosis. This agrees with the finding of Shin-S K et al, who found osteitis fibrosa cystica as the commonest type of renal osteodystrophy in predialysis patients studied in Canada (44.8% of total)<sup>4</sup>. Also Jarava-C et al found osteitis fibrosa cystica in 17 out of 20 haemodialysis patients in England with secondary hyperparathyroidism and renal osteodystrophy<sup>8</sup>. However, their findings were based on histological methods. This finding contradicts that of Coen-G et al, who found mixed osteodystrophy as the most predominant type in predialysis chronic renal failure patients in England<sup>9</sup>.

**4.3- Radiological features of renal osteodystrophy appear to be more prevalent in those with more advanced Chronic renal failure** -The 3 subjects with radiological evidence of renal osteodystrophy, belonged to group 3 (glomerular filtration rate ≤ 5mls/min) in the study.

All had duration of symptoms of chronic renal failure greater than 6 months. This is in agreement with the findings in England of Coen-G et al, who postulated that adynamic bone disease is commoner in early renal failure, and that osteomalacia and later osteitis fibrosa cystica tend to occur as resistance to parathyroid hormone develops, which occurs with increasing severity of chronic renal failure<sup>9</sup>. Radiological features appear late. Earlier features of renal osteodystrophy can be detected by bone biopsy or biochemical studies such as measurement of serum parathyroid hormone levels, which were not part of this work.

**4.4- There is no correlation between clinical features (bone pain) and radiological features -** A total of 11 patients (6 male and 5 female) had the symptom of bone pain. None had any radiological evidence of renal osteodystrophy. Instead all showed radiological evidence of osteoarthritis. Of the 3 patients who showed radiological evidence of renal osteodystrophy, none had the symptom of bone pain. This is in agreement with the finding of Hardousin-P et al, who found a high incidence of joint symptoms and radiological abnormalities in Canada, which could not with certainty be attributed to renal osteodystrophy<sup>10</sup>.

**4.5- Renal osteodystrophy appear more prevalent in females** 2 out of a total number of 34 females (5.88% of the female population) studied, showed radiological features of renal osteodystrophy, while only one male out of 56 (1.8% of the male population) studied, showed radiological evidence of renal osteodystrophy. Of the 3 radiologically positive subjects, 2 (66.7%) were female, while only one (33.3%) was male. This is in agreement with the findings of a study in England by Couttenye-M M et al, who concluded that women seem to be at higher risk of development of hyperparathyroidism, whereas aplastic bone disease has been related to the male gender in patients undergoing chronic ambulatory peritoneal dialysis<sup>11</sup>. This may in part be due to the effects of estrogens on osteoblasts. Osteoblasts have estrogen receptors, and respond to estrogens directly by producing growth factors. Thus, estrogens, like metabolic acidosis or nitric oxide deficiency have been postulated to potentiate the actions of parathyroid hormone on bone. It has been shown that estrogens also increase parathyroid hormone and calcitriol gene expression<sup>12</sup>.

In conclusion, we have shown that renal osteodystrophy, though uncommon, does exist in Nigerian Chronic renal failure patients. Osteitis fibrosa is the commonest form and it seems to be more prevalent in female patients. This may be

because, unlike in the recent past, Haemodialysis is now more readily available in Nigeria, leading to increasing longevity in Chronic renal failure patients. The low prevalence may in part, still reflect the relatively short duration of symptoms and poorer survival of these patients when compared to Western standards, because dialysis is relatively scarcer and unaffordable to most of the patients.

We recommend greater research interest in this field of nephrology, using more modern methods, to make a more accurate assessment of the gravity of this problem

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