UNIVERSITI PUTRA MALAYSIA

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PREVALENCE AND PATTERN OF RENAL OSTEODYSTROPHY AND ITS ASSOCIATION FACTORS AMONG CHRONIC DIALYSIS PATIENTS IN TWO-CENTER UNTIL JUNE 2013.

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ABSTRACT

Introduction: Renal osteodystrophy is the skeletal complication of end-stage renal disease which is a multifactorial disorder of bone remodelling which affects almost all patients with advance chronic kidney disease (CKD). In Malaysia, the number of dialysis patients is increasing but little information is available about their bone disorders.

Objectives: To describe the patterns of renal osteodystrophy and its association factors among chronic dialysis patients, and to compare the characteristics between hemodialysis and continuous ambulatory peritoneal dialysis (CAPD) in two centers, Serdang Hospital and Kajang Hospital.

Methods: We performed a cross sectional data collection, from medical records, for 281 patients doing maintenance dialysis in SerdangHospital and KajangHospital. Patients who had undergone total parathyroidectomy were excluded from the study. Blood investigations were done for all patients from HD and CAPD unit from January 2013 till June 2013. These biochemical parameters were recorded and analyzed using SPSS, version 21. Intact Parathyroid Hormone (iPTH) values and Serum Alkaline Phospatase (ALP) were used to determine Turnover Bone Disease (TOBD). For iPTH<150pg/ml and serum ALP <120 U/L classified as low bone turnover disease (LBTD), iPTH150-600 pg/ml and serum ALP 120-150 U/L as intermediate bone turnover disease (IBTD) and iPTH>600 pg/ml and serum ALP >150 U/L and as high bone turnover disease (HBTD).

Results: BothCAPD and HD had similar proportion of patients with corrected serum calcium-phosphate product less than 4.5 $mmol^2/L^2$, which was 80% for CAPD and 82.2% for HD. HD had better phosphate control with 23.4% patients achieved the target compared with CAPD with 19%. In CAPD, LBTD and HBTD had similar prevalence with 14.9% and 15.5% respectively. In HD, more patients were developed HBTD than LBTD with 29% vs 14%. There were no statistically significant associations between demographic characteristics (age, gender and ethnicity), dialysis duration, and co-morbidity status with pattern of renal osteodystrophy.

Conclusion: HBTD was more prevalent in HD patients while the prevalence of both LBTD and HBTD were similar in CAPD patients. There are no associations between demographic factors, dialysis duration, and co-morbidity status with pattern of renal osteodystrophy.

Keyword: Prevalence, renal osteodystrophy, Hemodialysis, Continuous Ambulatory Peritoneal Dialysis .

KELAZIMAN DAN CORAK OSTEODISTROFI GINJAL SERTA FAKTOR HUBUNG KAITNYA DALAM KALANGAN PESAKIT DIALISIS KRONIK DI 2 PUSAT DARI MAC SEHINGGA JUN 2013

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ABSTRAK

Pengenalan: Osteodistrofi ginjal (ROD) adalah merupakan komplikasi terhadap tulang rangka bagi pesakit yg menghidapi penyakit buah pinggang di peringkat akhir di mana ianya merupakan gangguan kepelbagaian faktor terhadap pembentukan semula tulang yang menjejaskan hampir semua pesakit dengan penyakit ginjal kronik. Ia adalah satu cabaran di seluruh dunia pada pesakit dialisis. Di Malaysia, bilangan pesakit dialisis meningkat tetapi sedikit maklumat boleh didapati tentang masalah tulang mereka.

Objektif: Tujuan utama kajian ini adalah untuk menentukan kekerapan dan corak ROD pada pesakit dialisis yg kronik di dua pusat, Hospital Serdang dan Hospital Kajang. Selain itu, kajian ini bertujuan untuk membandingkan corak ROD antara pesakit Hemodialisis (HD) dan Dialisis Peritoneum Ambulatori Berterusan (CAPD). Selain itu, kajian ini bertujuan untuk menentukan hubungan antara faktor demografi (umur, jantina, dan etnik) dan corak ROD, hubungan antara jenis dialisis dan corak ROD, hubungan antara tempoh dialisis dan corak ROD, dan hubungan antara morbiditi status dan corak ROD.

Kaedah: Kami melakukan pengumpulan data keratan lintang, dari rekod perubatan, bagi pesakit yang melakukan dialisis di Hospital Serdang dan Hospital Kajang. Pesakit yang telah menjalani pembuangan paratiroid telah dikecualikan daripada kajian ini. Penyiasatan darah dilakukan untuk semua pesakit dari HD dan CAPD unit dari Januari 2013 hingga Jun 2013. Parameter biokimia telah direkodkan dan dianalisis menggunakan SPSS, versi 21. Nilai hormon parathyroid utuh (iPTH) dan Serum Fosfat Alkali (ALP) telah digunakan untuk menentukan tahap Penyakit Tulang (TOBD). IPTH <150 pg/ml dan serum ALP <120 U/L dikelaskan sebagai perolehan tulang rendah, iPTH 150-600 pg/ml dan serum ALP 120-150 U/L sebagai perolehan tulang pertengahan, dan iPTH >600 pg/ml dan serum ALP >150 U/L sebagai perolehan tulang yang tinggi.

Hampir kajian : Kadar pembahagian pesakit dengan hasil serum kalsium-fosfat yang telah diperbetulkan iaitu < 4.5 $mmol^2/L^2$ untuk kedua-dua CAPD dan HD adalah hampir sama iaitu 80% CAPD dan 82.2% HD. HD mempunyai kawalan fosfat yang lebih baik dengan 23.4% pesakit mencapai target dibandingkan dengan 19% daripada pesakit CAPD. LBTD dan HBTD mempunyai kelaziman yang hampir sama dengan masing-masing 14.9% dan 15.5% dalam kalangan pesakit CAPD. Bagi pesakit HD, lebih banyak pesakit mengalami HBTD daripada LBTD dengan peratusan 29% vs

14%. Hubung kait antara karakter demografi (umur, jantina, etnik), tempoh dialisis, dan status ko-morbiditi dengan corak osteodistrofi ginjal ialah tiada nilai statistik yang signifikan.

Kesimpulan : Kelaziman penyakit tulang untuk pesakit HD adalah lebih kepada HBTD, manakala kelaziman untuk pesakit CAPD untuk kedua-dua LBTD dan HBTD adalah hampir sama. Tiada nilai statistik yang signifikan bagi hubung kait antara karakter demografi, tempoh dialisis, dan status ko-morbiditi dengan corak osteodistrofi ginjal.

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LIST OF ABBREVATION

CAPD	: Continuous Ambulatory Peritoneal Dialysis
CKD	: Chronic Kidney Disease
CKD-MBD	: Chronic Kidney Disease-Mineral and Bone Disorder
HD	: Hemodialysis
KDIGO	: Kidney Disease Improving Global Outcomes
MRTD`	: Malaysian Registry and Transplant Registry
NHANES	: National Health and Nutrition Examination Survey
ROD	: Renal Osteodystrophy

CHAPTER 1

INTRODUCTION

Renal osteodystrophy (ROD) is the disorder of the bone metabolism which affects almost all patients with advance Chronic Kidney Disease (CKD) or End Stage Renal Failure (ESRF). In this condition, there is elevation of the serum phosphorus level, low or normal serum calcium level, and stimulation of parathyroid function which result in a variable admixture of bone disease (Dorland, 2009).

In United Kingdom the prevalence of chronic kidney disease is approximately 600 individuals per million populations per year (0.06%). The incidence of end-stage renal failure is of the order of 200 per million populations per year (0.02%) (Baker, 1999). The overall prevalence of chronic kidney disease (CKD) in the adult population in the United States is 16.8% and after comparing the most recent National Health and Nutrition Examination Surveys (NHANES), it showed that the prevalence of chronic kidney disease (CKD) in the United States in 1999-2004 was higher than in 1988-1994 (Coresh et al, 2007)

Renal osteodystrophy (ROD) is the common complication of end-stage renal failure and maintenance dialysis treatment (Gerakis, 1996). There are two patterns of ROD, which are high bone turnover disease (HBTD) and low turnover bone disease (LBTD) (Eknoyan et al, 2003). Another histological pattern of ROD also includes mixed or intermediate renal osteodystrophy, which both elements of high and low turnover might be seen (Michael, 2003). Parathyroid hormone (PTH) level is considered a useful test in detecting high and low turnover bone disease (Eknoyan et al, 2003). In this study, Intact Parathyroid Hormone (iPTH) and Serum Alkaline Phosphatase (ALP) values were used to determine Turnover Bone Disease (TOBD).

For iPTH, < 150 pg/ml classified as low bone turnover, 150-600 pg/ml as intermediate or mixed bone turnover and, >600 pg/ml as high bone turnover. For serum ALP, < 120 U/L classified as low bone turnover, 120-150 U/L as intermediate bone turnover and, >150 U/L as high bone turnover (20TH Report of The Malaysian Dialysis & Transplant Registry 2012).

In the clinical setting especially in the chronic kidney disease (CKD), Hemodialysis (HD) and Continuous Ambulatory Peritoneal Dialysis (CAPD) are the main type of dialysis that had been used in Malaysia (Lim et al, 2000). Prevalence and patterns of ROD between Hemodialysis (HD) and Continuous Ambulatory Peritoneal Dialysis (CAPD) in local setting, was our main interest in this research.

1.1 PROBLEM STATEMENT

In Malaysia, the incidence and prevalence of patients with end stage renal disease (ESRD) on dialysis had increased from 88 and 325 per million population respectively in 2001 to 170 and 762 population respectively in 2009 (Lim, 2011). Based on 20th Report of Malaysian Dialysis and Transplant Disease 2012, about 40% of dialysis patients developed into low bone turnover disease (LBTD) and high bone turnover disease (HDTD).

1.2SIGNIFICANCE OF STUDY

This study will help to determine the characteristic features of ROD patients that most probability develops high turnover bone disease (HBTD) and low turnover bone disease (LBTD). This will help the healthcare service providers to increase

awareness regarding ROD. This study also will help clinician to recognize pattern of ROD in HD and CAPD maintenance patients.

1.3 OBJECTIVE

1.3.1 General objective

To ascertain the prevalence and pattern of renal osteodystrophy (ROD) among chronic dialysis patients in Serdang Hospital and Kajang Hospital.

1.3.2 Specific objectives

1. To determine demographic characteristics, co-morbidity status, biochemical parameters, and medication distributions of Continuous Ambulatory Peritoneal Dialysis (CAPD) and Hemodialysis (HD) patients
2. To compare the demographic characteristics, co-morbidity status, biochemical parameters and medication distributions between CAPD and HD patients.
3. To compare the pattern of ROD between CAPD and HD group.
4. To determine the association between demographic factors and pattern of ROD among CAPD and HD patients.
5. To determine the association between duration of dialysis and pattern of ROD among CAPD and HD patients.
6. To determine the association between co-morbidity status and pattern of ROD among CAPD and HD patients.

1.4 RESEARCH HYPOTHESIS

1. There is an association between demographic factors and pattern of ROD among CAPD and HD.

2. There is an association between dialysis duration and pattern of ROD among CAPD and HD.

3. There is an association between co-morbidity status and pattern of ROD among CAPD and HD.

CHAPTER 2

LITERATURE REVIEW

2.1 Renal osteodystrophy, chronic kidney disease (CKD) and CKD-MBD

Renal osteodystrophy, as defined by The National Institutes of Health Consensus Conference, is a histomorphometrically defined complex group of skeletal disorders caused by chronic kidney disease (CKD). Clinical and histologic forms of renal osteodystrophy includes predominantly high turnover states, such as hyperparathyroid bone disease (HP). Mixed bone disease (MBD), low turnover osteomalacia (OM), and adynamic bone disease (ABD) (Holanda et al, 2003).

To address the expanded understanding of the complex systemic impact of chronic kidney disease (CKD), a working group of the National Kidney Foundation, Kidney Disease Improving Global Outcome (KDIGO) came out with the term CKD-MBD (chronic kidney disease-mineral and bone disorder) which defined as a systematic disorder of mineral and bone metabolism due to chronic kidney disease (CKD) that manifested by one or a combination of : abnormalities of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D metabolism; abnormalities in bone turnover, mineralization, volume, linear growth, or strength; vascular or soft tissue calcification (Moe et al, 2010).

2.1.1 Prevalence of chronic kidney disease (CKD)

The overall prevalence of chronic kidney disease (CKD) in the adult population in the United States is 16.8% and after comparing the most recent National Health and Nutrition Examination Surveys (NHANES), it showed that the prevalence of chronic kidney disease (CKD) in the United States in 1999-2004 was higher than in

1988-1994 (Coresh et al, 2007). In Malaysia, the incidence and prevalence of patients with end stage renal disease (ESRD) on dialysis had increased from 88 and 325 per million population respectively in 2001 to 170 and 762 population respectively in 2009 (Lim, 2011). The increase in end stage renal disease (ESRD) was largely associated with the increasing incidence of diabetic kidney disease (DKD) accounting for 58% of new patients accepted for dialysis (Lim, 2011).

2.2 Renal osteodystrophy (ROD)

Renal osteodystrophy is a condition due to chronic kidney disease and renal failure with the elevation of the serum phosphorus level, low or normal serum calcium level, and stimulation of parathyroid function which result in a variable admixture of bone disease (Dorland, 2009).

2.2.1 Pattern of renal osteodystrophy

The high bone turnover disease (HBTD) characterised by increase in the number of osteoblasts and osteoclasts with high rate of bone formation due to secondary hyperparathyroidism (Fukugawa, 2002). A few patients develop secondary hyperparathyroidism in which the parathyroid hormone (PTH) level increase dramatically and will continue to elevate even with restoration of the serum calcium level back to normal. They prone to develop hypercalcemia with the usual replacement dose of calcium, in which sometimes referred as tertiary hyperparathyroidism (Shoback et al, 2001). There are many factors that influence the over activity of parathyroid glands which include; retention of phosphorus, decrease in the level of calcitriol, and intrinsic alteration within the parathyroid that give rise to increase parathyroid hormone (PTH) secretion as well as increase parathyroid growth, skeletal

resistance to the action of parathyroid hormone (PTH) and hypocalcaemia. Histological findings of high turnover bone disease also called osteitis fibrosa (Fukagawa, 2002).

Another pattern of ROD is low bone turnover disease (LBTD) which is characterized by reduced osteoblasts and osteoclasts, and there is no accumulation of osteoid. LBTD is observed in patient with kidney disease, especially in patient who are on dialysis and is characterised by extremely slow rate of bone formation. LBTD includes osteomalacia and the most common one is adynamic bone disease (Coen et al, 1998). Osteomalacia in HD patients is mostly due to a consequence of aluminium intoxication, while adynamic bone disease is a term which describes a histological pattern of ROD that were found to be unrelated to aluminium accumulation in most cases (Coen et al, 1998).

The histological pattern of bone disease also includes mixed renal osteodystrophy. Mixed renal osteodystrophy is said to occur when both abnormalities of increased production of osteoid in hyperparathyroid and reduced mineralization in osteomalacia are found (Michael, 2003).

2.2.2 Prevalence of renal osteodystrophy

Some research has been done on the prevalence of renal osteodystrophy (ROD). Regarding the prevalence of ROD on HD patients, Sanusi et al (2010) stated that ROD in patients with end-stage renal disease (ESRD) is associated most commonly with low bone turnover disease (LBTD) while occurrence of hyperparathyroid bone disease appeared low. Research by Buargub M. A et.al (2006) in Libya found that the prevalence of ROD among chronic HD patient was 55.3%. From that proportion, 29 (28.1%) had laboratory evidence of hyperparathyroid bone

disease, while 28 patients (27.1%) had laboratory evidence of adynamic bone disease. In only 18 patients, (17.4%) the serum levels of iPTH were within the target range recommended by the K/DOQI guidelines (150-300 pg/ml).

In the latest study done in Nigeria, it was found that 78% of the chronic renal failure patients had raised level of total serum alkaline phosphatase which correlates well with parathyroid hormone (PTH) level. About 66% of them histologically had osteitis fibrosa. Thus, they concluded that the commonest type of ROD is osteitis fibrosa, which is the form of HBTD (Onyemekeihia, 2012).

2.3 Biochemical markers

Many studies agreed that biochemical markers should be monitored as a major role in investigating renal osteodystrophy (ROD). Gerakis et al (1996) stated that bone biopsy could remain as the gold standard for diagnosis of ROD. According to Fletcher et al (1997), bone biopsy is undeniably could accurately predict ROD, but this method is an invasive procedure and unsuitable for repeated routine use.

In recent years a great number of biochemical markers have been developed which allow determining more precisely the evolution of bone turnover (Alvarez L. et al, 2004). Measurement of parathyroid hormone (PTH) has been widely used since parathyroid hormone (PTH) is a major regulatory of bone turnover and skeletal cellular activity (Pei, 1995). The predictive power of parathyroid hormone levels is increased by concomitant consideration of alkaline phosphatase (KDIGO).

The other important biochemical markers are calcium and phosphate. Corrected serum phosphate should be achieved to avoid hyperphosphatemia (Block, 1998).

2.4 Medications

Phosphate binder is the second line therapy when dietary phosphate restriction is inadequate to control serum levels of phosphorus and parathyroid hormone (KDOQI). Phosphate binders are recommended to lower serum phosphate and will prevent the hyperphosphatemia among chronic kidney disease (CKD) disease. The examples of phosphate binders are the calcium–based phosphate binders and non-calcium-based phosphate. Non-calcium based phosphate binders are associated with a lower risk for all-cause mortality in patients with chronic kidney disease (Sophie et al, 2013).

Regarding some research, they find that vitamin D supplementation appears to improve 25(OH)D and $1,25(OH)_2D$ levels while reducing PTH levels without increasing the risk for hypercalcemia and hyperphosphatemia.(Praveen et al, 2010).

2.5 Dialysis

The principal role of the kidneys is the filtration and removal of waste products and excess fluid from the blood. Dialysis is a way of replacing kidney function in people whose kidneys have failed. There are two main forms of dialysis; Hemodialysis (HD) and Continuous Ambulatory Peritoneal Dialysis (CAPD) (Kidney Research UK, 2006). Hemodialysis and Peritoneal Dialysis remove waste, salt and extra water to prevent them from building up in blood. Both also keep a safe level of certain chemicals in blood and help to regulate blood pressure (National Kidney Foundation, 2007).

2.5.1 Hemodialysis (HD)

Hemodialysis (HD) is the most common method used to treat advanced and permanent kidney failure for many years. When kidneys fail, HD allows blood to flow, a few ounces at the time, through a special filter that removes wastes and extra fluids (National Institute of Diabetes and Digestive and Kidney disease/NIDDK, 2006). In HD, blood is taken from the patient's circulation, passed through an artificial kidney, and returned to the patient. HD machine has a special filter called a dialyzer. It functions to clean blood. To get the blood into the dialyzer, the doctor needs to make an access, or entrance, into blood vessels. This is done with minor surgery, usually to arm. The dialyzer, or filter, has two parts. One part for blood and the other part for a washing fluid called dialysate (National Kidney Foundation, 2007).

2.5.2 Continuous ambulatory peritoneal dialysis (CAPD)

In Peritoneal Dialysis, the internal lining of the abdomen acts as the artificial kidney. During Peritoneal Dialysis, fluid is drained into the peritoneal cavity, allowed to sit there for several hours whilst it absorbs waste products, and then drained out. This process, repeated several times a day, can effectively replace kidney function and - because it is a continuous process which allows you to carry on with normal activities - it is known as Continuous Ambulatory Peritoneal Dialysis (CAPD) (Kidney Research UK, 2006).

2.6 Hemodialysis (HD) versus continuous ambulatory peritoneal dialysis (CAPD)

Recent studied had shown some differences outcome between Hemodialysis (HD) and Continuous Ambulatory Peritoneal Dialysis (CAPD). The prevalence of high bone turnover in HD patients was significant higher compare to CAPD (Yanova D & Dukova P, 2004). Besides, there were also significantly higher of biochemical markers in the HD patients compared to the CAPD-. It showed some increasing in the value of intact Parathyroid Hormone (iPTH), bone alkaline phosphatase (BAP), osteocalcin (OS), dioxipyridinolyne (DYP) (G Hampson et al, 2002). The increasing in the value of intact Parathyroid hormone (iPTH) shows association with high bone turnover in HD patients (Wang M et al, 1995). In certain study, they proved that higher prevalence of high bone turnover was reported among patients on HD and higher prevalence of low bone turnover was reported among patients on CAPD (Sherrard et al, 1993). Moreover, in the CAPD there are high effects on bone mineral density compared to HD. They found that the CAPD prone to conserve cortical bone compared to HD (Csaba Ambrus et al, 2010).

2.7 Factor associated with pattern of renal osteodystrophy

2.7.1 Gender

Earlier research by Couttenye et al (1997) was showed that women seemed to develop high bone turnover disease (HBTD) whereas men seemed to more frequently develop high bone turnover disease (HBTD). However, Odenigbo et al (2003) was found that ROD more prevalent in females. The latest report by 20th Report of Malaysian Dialysis and Transplant Registry 2012 stated that slightly more male had LBTD but no gender difference was noticed for HBTD.

2.7.2 Age

In the Unites States, the average age of the patient undergoing dialysis has been increasing over the last several decades. In 2000, the average age was approximately 62 years old. (Hansberry et al, 2005). Some study had showed that high bone turnover may be sustained well into advanced age. (Marcus, 2006)

2.7.3 Co-morbidities

From 20th Report of Malaysian Dialysis and Transplant Registry 2012, patients with diabetes had relatively lower level of iPTH compared to patients with no diabetes for both CAPD and HD group. Therefore, high bone turnover diseases (HBTD) were seen more in non-diabetes patients compared to diabetes patients.

2.7.4 Dialysis duration

Research from Onyemekeihia et al (2012) found that patients that had histological evidence of ROD with elevation of serum alkaline phosphatase had an association with the long-time period of dialysis. It had been one of the contributing factors that might affect the prevalence of pattern of ROD.

2.7.5 Dialysis type

The serum levels of parathyroid hormone (PTH) and alkaline phosphatase were not significantly different although it was lower in Continuous Ambulatory Peritoneal Dialysis (CAPD) than Hemodialysis (HD) patients (Torres et al, 1995). 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012 reported that more HD patients suffered both low bone turnover disease (LBTD) (30%) and high bone turnover disease (HBTD) (4-6%) compared to CAPD (LBTD was 3% and HBTD were 0-1%).

2.8 Conceptual framework

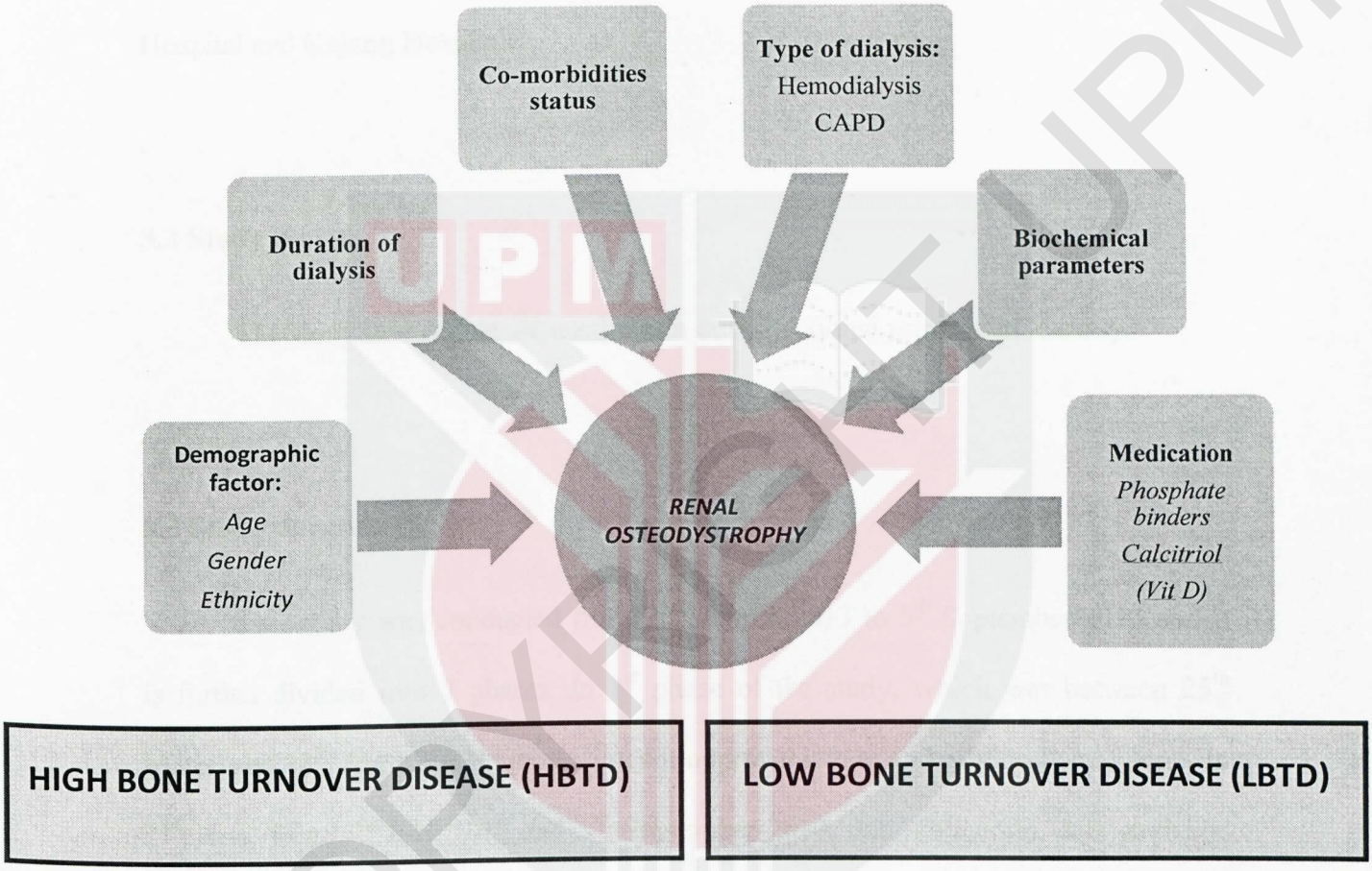

Figure 1: Conceptual framework

CHAPTER 3

METHODOLOGY

3.1 Study location

The study was conducted in the Hemodialysis unit in two centres, Serdang Hospital and Kajang Hospital.

.

3.2 Study design

The study design that we used was a cross-sectional retrospective study.

3.3 Study duration

This study was conducted from 25th March 2013 to 5th September 2013 and it is further divided into 2 phases. In 1st phase of the study, which was between 25th March and 18th April 2013, preparation for approval letters and proposal were done. In 2nd phase, from 5th July 2013 and 5th September 2013, data collection, data analysis, scientific articles and final report will be done.

3.4 Sampling

3.4.1 Study population

Study population were all the patients of chronic kidney disease that admitted on Hemodialysis unit in Serdang and Kajang Hospital from until June 2013.

3.4.2 Sampling population

The sampling population were the patients of chronic kidney disease that still undergoing Hemodialysis (HD) and Continuous Ambulatory Peritoneal Dialysis (CAPD) in Serdang Hospital and Kajang Hospital until June 2013.

3.4.2.1 Inclusion criteria

All records of patients of chronic kidney disease who were still on HD and CAPD until June 2013 in Serdang Hospital and Kajang Hospital.

3.4.2.2. Exclusion criteria

All patients who already underwent parathyroidectomy.

3.4 3 Sampling frame

List of patients of chronic kidney disease that still undergo HD and CAPD in Serdang Hospital and Kajang Hospital until June 2013.

3.4.4 Sampling unit

Record of one patient of chronic kidney disease who was undergo HD and CAPD in Serdang Hospital and Kajang Hospital that fulfilled the inclusion and exclusion criteria.

3.4.5 Sampling method

The sampling method for this study was universal sampling. We took all the patients of chronic kidney disease who was on Hemodialysis (HD) and Continuous Ambulatory Peritoneal Dialysis (COPD) in Serdang Hospital and Kajang Hospital until June 2013.

3.4.6 Sample size

The formula that was used to calculate sample size estimation:

$$n = \frac{z^2_{1-a/2}[P_1(1-P_1)+P_2(1-P_2)]}{d^2}$$

Where

P_1 = Prevalence of high turnover bone disease

= 0.281 (M. A. Buargub, 2006)

P_2 = prevalence of low turnover bone disease

= 0.273 (M. A. Buargub, 2006)

d = desired proportion

$z^2_{1-a/2}$ = 1.96 with 95% confidence interval

$$n = \frac{1.96[0.281(0.719)+0.271(0.729)]}{(0.06)^2}$$

n = 218 subjects

Total minimum sample size in this study was 218 subjects.

Estimation of missing data during collection = 10%. So,

10%x 218=22

≈ 22 subjects

Then, 22+218=240subjects.

So, estimation sample size in our study was 240 subjects.

3.5 Instruments and data collection

3.5.1 Instruments

Standardized proforma were used to extract the data from the secondary data which were data sheets of patients of chronic kidney disease who was currently on regular HD and CAPD in Serdang Hospital and Kajang Hospital which covered their level of biochemical markers until June 2013.

3.5.2 Data collection techniques

Data were retrieved from available medical reports of patients in Serdang Hospital and Kajang Hospital in Hemodialysis Unit based on the patient's data on age, sex, ethnicity, duration of dialysis, primary disease of the patient and also their biochemical markers level which are calcium (Ca), alkaline phosphatase (ALP), phosphate (P), intact parathyroid hormone (iPTH), calcium carbonate ($CaC0_3$), and vitamin D by using standardized proforma. Calcium carbonate is used to determine the phosphate binders among the patients as medication.

3.6 Data analysis

Firstly, univariate descriptive analysis was carried out to identify the distribution of the sample population with respect to demographic factor, dialysis duration, and co-morbidity status by determining the frequency and percentage of each variable for both CAPD and HD group. For biochemical parameters and medications, we determined the mean and standard deviation, so that we can compare it between CAPD and HD group. After that, bivariate or multivariate analyses between pattern of ROD and demographic factor, dialysis duration and co-morbidity status were carried out. Data analysis was performed using the statistics software SPSS version 21. We performed chi-square test to present the association of socio demographic factors, dialysis duration, and co-morbidity status of patients, with pattern of ROD.

A p value less than 0.05 were considered significant.

3.7 Study ethics

Ethical form was submitted to the following individuals /institution:

a) The Ethical Committee of Faculty of Medicine and Health Science,Universiti Putra Malaysia

b) Clinical Research Centre (CRC)

c) The National Institute of Health (NIH)

d) Medical Research Ethical Committee (MREC)

Approval letter was written to the following institution:

a) Director of Hospital Serdang and Hospital Kajang.

3.8 Variables

3.8.1 Dependent variables

Pattern of renal osteodystrophy (ROD)

3.8.2 Independent variables

1. Demographic factor (age, gender, ethnicity)

2. Biochemical parameters and medication

3. Dialysis type

4. Duration of dialysis

5. Co-morbidity status

3.9 Definition of term

1) Renal osteodystrophy: Changes in mineral metabolism and bone structure develop early in the course of chronic kidney disease (CKD).
2) Dialysis: A way of replacing kidney function in people whose kidneys have failed.
3) Osteitis fibrosa: Increasing of bone turnover due to hyperparathyroidism. Also called as high bone turnover disease (HBTD). Diagnosed if the iPTH level is >600 pg/ml combined with ALP level >150 U/L.
4) Adynamic bone disease: low bone turnover cause by excessive suppression of parathyroid glands and aluminium deposition. Also known as low bone turnover disease (LBTD). Diagnosed if the iPTH level <150 pg/ml combined with ALP <120 U/L.
5) Osteomalacia: low bone turnover in combination with an increased volume of unmineralized bone. Also known as intermediate bone turnover disease (IBTD). Combination of iPTH level 150-600 pg/ml and ALP LEVEL 120-150 U/L.
6) Mixed renal osteodystrophy : may seen both high and low turnover elements.
7) Biochemical markers: detected in urine, blood, or other body fluids that serve as a sign of a disease or abnormality. Examples; phosphate (PO4), calcium (Ca), alkaline phosphatise (ALP), and intact parathyroid hormone (iPTH).

CHAPTER 4

RESULT

4.1 RESPONSE RATE

The total number of patients who fulfilled the inclusion and the exclusion criteria was 281. Our sample size is 240. Since we are used universal sampling, so we took all 281 patients and they were reviewed and recorded.

4.2 DESCRIPTIVE DATA ANALYSIS (DISTRIBUTION)

4.2.1 Distribution of socio demographic, biochemical parameters, and medication on Coninuous Ambulatory Peritoneal Dialysis (CAPD) patients.

Table 1 shows distribution of 174 Continuous Ambulatory Peritoneal Dialysis (CAPD) patients. For Continuous Ambulatory Peritoneal Dialysis (CAPD group), mean age was 50.53 ± 15.96 years. Male (45.4%) patients were higher than female (54.6%). In ethnicity, Malay patients were dominated with 62.1%, followed by Chinese (29.9%), Indian (7.5%) and others (0.6%). For the duration of dialysis, 86.8% of patients were on dialysis duration in less than 5 years and 13.2% of them were in more than 5 years.

Primary disease for End Stage Renal Disease (ESRD) patients mainly was Diabetes Mellitus (53.4%), followed by hypertension (29.3%), Glomerulonephritis (10.9%), unknown (5.2%) and others (1.1%).

Table 1: Demographic characteristic of Continuous Ambulatory Peritoneal Dialysis (CAPD) patients in Serdang Hospital and Kajang Hospital.

Characteristics	Mean ± SD	Number (n)	Percentage (%)
Gender			
Male		79	45.4
Female		95	54.6
Age (years)	50.53 ± 15.96		
Ethnicity			
Malay		108	62.1
Chinese		52	29.9
Indian		13	7.5
Others		1	0.6
Primary disease			
Diabetes mellitus		93	53.4
Hypertension		51	29.3
Glomerulonephritis		19	10.9
Others		2	1.1
Unknown		9	5.2
Duration dialysis			
<5 years		151	86.8
≥5 years		23	13.2

Table 2 shows the biochemical distribution of CAPD group. Mean values for biochemical parameters showed serum Calcium 2.11 ± 0.28mmol/L, serum Phosphate 1.67 ± 0.52mmol/L, Calcium Phosphate Product (mmol/L) 3.51 ± 1.15, serum Alkaline Phosphatase (ALP)134.84 ± 107.98 U/L, serum intact parathyroid hormone (iPTH) 545.72± 556.63 pg/ml.19% of Continuous Ambulatory Peritoneal Dialysis (CAPD) patients achieved the target phosphate level by Kidney Disease Improving Global Outcomes (KDIGO) (0.8-1.3 mmol/L) and 81% were not achieved it. For the corrected Calcium Phosphate Product (<4.5 $mmol^2/L^2$), 80.5% of them were achieved the target while the other 19.5% were not achieved.

Table 2: Biochemical distribution of Continuous Ambulatory Peritoneal Dialysis (CAPD) patients in Serdang Hospital and Kajang Hospital.

	Mean ± SD	Number (n)	Percentage (%)
Biochemical parameters:			
Ca (mmol/L)	2.11 ± 0.28		
PO4 (mmol/L)	1.67 ± 0.52		
CaPO4 product (mmol/L)	3.51 ± 1.15		
iPTH (pg/ml)	545.72 ± 556.63		
ALP (U/L)	134.84 ± 107.98		
Hb (g/dL)	10.17 ± 1.89		
Alb (g/L)	29.5 ± 6.76		
Target phosphate level (0.8-1.3 mmol/L		33	19.0
Achieved		141	81.0
Not achieved			
Corrected CaPO4 product (<4.5 $mmol^2/L^2$)			
Achieved		140	80.5
Not achieved		34	19.5

Table 3 shows the distribution of medication among CAPD group. For the medication, 90.8% of them used calcium carbonate and 9.2% used non calcium carbonate binder, i.e Lanthanum. Most of the patients were taken Vitamin D (88.5%).

Table 3: Medication distribution of Continuous Ambulatory Peritoneal Dialysis (CAPD) patients in Serdang Hospital and Kajang Hospital.

Medication	Mean ± SD	Number (n)	Percentage (%)
Phosphate binder			
Calcium carbonate	1.13 ±1.39	158	90.8
Non Calcium carbonate		16	9.2
Vitamin D		154	8.5

4.2.1 Distribution of socio demographic, biochemical parameters, and medication on Hemodialysis (HD) patients.

Table 4 shows the distribution of 107 Hemodialysis (HD) patients. Mean age for this group was 54.70 ± 13.86 years. Male distribution was higher than female with 54.2% versus 45.8%. Chinese were dominated in this group with 44.9%, followed by Malay (42.1%), and Indian (13.1%). For the duration of dialysis, more patients in Hemodialysis (HD) group were doing dialysis for more than 5 years with 66.4% and only 33.6% of them were doing dialysis for less 5 years.

For the Hemodialysis (HD) group, primary disease for End Stage Renal Disease (ESRD) also mainly was Diabetes Mellitus (39.3%), followed by hypertension (25.2%), unknown (18.7%), others (10.3%) and lastly, Glomerulonephritis (6.5%).

Table 4: Demographic characteristics of Hemodialysis (HD) patients in Serdang Hospital and Kajang Hospital.

Characteristics	Mean ± SD	Number (n)	Percentage (%)
Gender			
Male		58	54.2
Female		49	45.8
Age (years)	54.70 ± 13.86		
Ethnicity			
Malay		45	42.1
Chinese		48	44.9
Indian		14	13.1
Others		0	0
Dialysis duration (years)			
< 5 years		36	33.6
≥5 years		71	66.4
Primary disease			
Diabetes Mellitus		42	39.3
Hypertension		27	25.2
Unknown		20	18.7
Others		11	10.3
Glomerulonephritis		7	6.5

Table 5 shows the distribution of biochemical parameters of HD patients. Mean values for biochemical parameters showed serum calcium 2.11 ± 0.28mmol/L, serum phosphate 1.54 ± 0.53mmol/L, calcium phosphate product (mmol/L) 3.42±1.25, serum alkaline phosphatase (ALP) 153.96 ± 109.69 U/L, serum intact parathyroid hormone (iPTH) 1517.87± 3421.4 pg/ml. 23.4% achieved the target phosphate level by Kidney Disease Improving Global Outcomes (KDIGO) (0.8-1.3 mmol/L), and 76.6% not achieved target phosphate level. For the corrected calcium phosphate product (<4.5 $mmol^2/L^2$), 82.2% achieved and 17.8% not achieved.

Table 5: Biochemical parameters distribution of Hemodialysis (HD) patients in Serdang Hospital and Kajang Hospital.

Characteristics	Mean ± SD	Number (n)	Percentage (%)
Biochemical parameters:			
Hb (g/dL)	10.64 ± 1.81		
Ca (mmol/L)	2.21 ± 0.28		
PO4 (mmol/L)	1.54 ± 0.53		
CaPO4	3.42±1.25		
product(mmol/L)	1517.87± 3421.4		
iPTH (pg/ml)	153.96 ± 109.69		
ALP (U/L)	35.78 ± 6.10		
Alb (g/L)			
Target phosphate level (0.8-1.3 mmol/L		25	23.4
Achieved		82	76.6
Not achieved			
Corrected CaPO4 product (<4.5 mmol^2/L^2)		88	82.2
Achieved		19	17.8
Not achieved			

Table 6 shows the medication distribution of HD patients. For medication distributions, majority of them (91.6%) also used calcium carbonate as phosphate binder, while 8.4% were used non calcium carbonate as phosphate binders. In Hemodialysis (HD) group, 71% of them took the Vitamin D.

Table 6: Medication distribution of the Hemodialysis (HD) patients in Serdang Hospital and Kajang Hospital

Medication	Mean ± SD	Number (n)	Percentage (%)
Phosphate binders	33.57±139.61		
Calcium carbonate		98	91.6
Non calcium carbonate		9	8.4
Vitamin D		70	71.0

4.3 PREVALENCE OF PATTTERN OF RENAL OSTEODYSTROPHY (ROD)

Table 7 shows the prevalence of pattern of ROD among Continuous Ambulatory Peritoneal Dialysis (CAPD) group. The prevalence of low bone turnover disease (LBTD) and high bone turnover disease (HBTD) were almost the same with 14.8% and 15.5% respectively. Intermediate bone turnover disease (IBTD) was the highest prevalence.

Table 7: Prevalence of pattern renal osteodystrophy (ROD) among Continuous Ambulatory Peritoneal Dialysis (CAPD) group.

Characteristics	Mean ± SD	Number	Percentage
Renal Osteodystrophy			
LBTD		26	14.9
IBTD		121	69.5
HBTD		27	15.5

Table 8 shows the prevalence of pattern of ROD among Hemodialysis (HD) group. Prevalence of high bone turnover disease (HBTD) was higher than low bone turnover disease (LBTD) with 29% versus 14%. Intermediate bone turnover disease (IBTD) still was the highest prevalence in Hemodialysis (HD) patients.

Table 8: Prevalence of pattern renal osteodystrophy (ROD) among Hemodialysis (HD) group

Characteristics	Mean ± SD	Number	Percentage
Renal Osteodystrophy			
LBTD		15	14
IBTD		61	57
HBTD		31	29

4.4 ANALYTICAL ANALYSIS OF CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD) GROUP AND HEMODIALYSIS (HD) GROUP

4.4.1. Association between demographic characteristics and pattern of renal osteodystrphy (ROD) among Continuous Ambulatory Peritoneal Dialysis (CAPD) and Hemodialysis (HD) group

4.4.1.1 Association between gender and pattern of renal osteodystrophy (ROD)

Table 9 shows the association of gender with pattern of renal osteodystrophy among Continuous Ambulatory Peritoneal Dialysis (CAPD) group. The results showed there is no significant association between gender of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 1.946, p = 0.378$].

Table 9: Association between gender and pattern of renal osteodystrophy in Continuous Ambulatory Peritoneal Dialysis (CAPD) patients

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	χ2	df	p-value
Gender:						
Male	15 (19.0)	53 (67.1)	11 (13.9)	1.946	2	0.378
Female	11 (11.6)	68 (71.6)	16 (16.8)			

Chi square test

Table 10 shows the association of gender with pattern of renal osteodystrophy among Hemodialysis (HD) group. The results showed there is no significant association between gender of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 1.472$, $p = 0.479$].

Table 10: Association between gender and pattern of renal osteodystrophy (ROD) among Hemodialysis (HD) patients.

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	χ2	df	p-value
Gender:						
Male	9(15.5)	35(60.3)	14(24.1)	1.472	2	0.479
Female	6(12.2)	26(53.1)	17(34.7)			

Chi- square test

4.4.1.2 Association between ethnicity and pattern of renal osteodystrophy (ROD)

Table 11 shows the association of ethnicity with pattern of renal osteodystrophy among Continuous Ambulatory Peritoneal Dialysis (CAPD) group.The results showed there is no significant association between ethnicity of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 2.691$, $p = 0.847$].

Table 11: Association between ethnicity and pattern of renal osteodystrophy among Continuous Ambulatory Peritoneal Dialysis (CAPD) group

	Low bone activity n (%)	Intermediate bone activity n (%)	High bone activity n (%)	χ2	df	p-value
Ethnic:						
Malay	14 (13.0)	79 (73.1)	15 (13.9)	2.691	6	0.847
Chinese	10 (19.2)	32 (61.5)	10 (19.2)			
Indian	2 (15.4)	9 (69.2)	2 (15.4)			

Chi square test

Table 12 shows the association of ethnicity with pattern of renal osteodystrophy among Hemodialysis (HD) group.The results showed there is no significant association between ethnicity of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 1.837$, $p = 0.766$].

Table 12: Association between ethnicity and pattern of renal osteodystrophy among Hemodialysis (HD) patients.

	Low bone activity n (%)	Intermediate bone activity n (%)	High bone activity n (%)	χ2	df	p-value
Ethnic:						
Malay	6(13.3)	23(51.1)	16(35.6)	1.837	4	0.766
Chinese	7(14.6)	30(62.5)	11(22.9)			
Indian	2(14.3)	8(57.1)	4(28.6)			

Chi-square test

4.4.1.3 Association between age and pattern of ROD

Table 13 shows the association of age with pattern of renal osteodystrophy among Continuous Ambulatory Peritoneal Dialysis (CAPD) group. The results showed there is no significant association between age of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 4.606$, $p = 0.100$].

Table 13: Association between age and pattern of renal osteodystrophy in Continuous Ambulatory Peritoneal Dialysis (CAPD) group

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	χ2	df	p-value
Age						
<60 years	14(12.1)	80 (69.0)	22 (19.0)	4.606	2	0.100
≥60 years	12 (20.7)	41 (70.7)	5 (8.6)			

Chi-square test

Table 14 shows the association of age with pattern of renal osteodystrophy among Hemodialysis (HD) group. The results showed there is no significant association between age of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 3.214$, $p = 0.200$].

Table 14 : Association between age and pattern of renal osteodystrophy among Hemodialysis (HD) group.

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	χ2	df	p-value
Age						
<60 years	6(9.5)	36(57.1)	21(33.3)	3.214	2	0.2
≥60 years	9(20.5)	25(56.8)	10(22.7)			

Chi-square test

4.4.2. Association between dialysis duration and pattern of renal osteodystrophy (ROD)

Table 15 shows the association of duration of dialysis with pattern of renal osteodystrophy among Continuous Ambulatory Peritoneal Dialysis (CAPD) group. The results showed there is no significant association between duration of dialysis of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 2.672$, $p = 0.263$].

Table 15: Association between dialysis duration and pattern of renal osteodystrophy among Continous Ambulatory Peritoneal Dialysis (CAPD) group.

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	$\chi 2$	df	p-value
Duration						
<5 years	24 (15.9)	106 (70.2)	21 (13.9)	2.672	2	0.263
≥5 years	2 (8.7)	15 (65.2)	6 (26.1)			

Chi-square test

Table 16 shows the association of duration of dialysis with pattern of renal osteodystrophy among Hemodialysis (HD) group. The results showed there is no significant association between duration of dialysis of patients with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 0.318$, $p = 0.853$].

Table 16: Association between dialysis duration and pattern of renal osteodystrophy (ROD) among Hemodialysis (HD) group

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	χ2	df	p-value
Duration						
<5 years	6(16.7)	20(55.6)	10(27.8)	0.318	2	0.853
≥5 years	9(12.7)	41(57.7)	21(29.6)			

Chi square test

4.4.3. Association between co-morbidity status and pattern of renal osteodystrophy (ROD)

Table 17 shows the association of co-morbidities status with pattern of renal osteodystrophy among Continuous Ambulatory Peritoneal Dialysis (CAPD) group. The results showed there is no significant association between co-morbidities status with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 3.787$, $p = 0.151$].

Table 17: Association between co-morbidities status and pattern of renal osteodystrophy among Continuous Ambulatory Peritoneal Dialysis (CAPD) group.

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	$\chi 2$	df	p-value
Primary disease:				3.787	2	0.151
Diabetes	16 (17.2)	67 (72.0)	0 (10.8)			
Non diabetes	10 (12.3)	54 (66.7)	17 (21.0)			

Chi square test

Table 18 shows the association of co-morbidities status with pattern of renal osteodystrophy among Hemodialysis (HD) group. The results showed there is no significant association between co-morbidities status with the pattern of renal osteodystrophy as the *p*-value is more than 0.05 [$\chi 2 = 0.008$, $p = 0.996$].

Table 18: Association between co-morbidities status and pattern of renal osteodystrophy among Hemodialysis (HD) group.

	Low bone turnover n (%)	Intermediate bone turnover n (%)	High bone turnover n (%)	χ2	df	p-value
Primary disease:				0.008	2	0.996
Diabetes mellitus	6 (14.3)	24 (57.1)	12 (28.6)			
Non diabetes	9 (13.8)	37 (56.9)	19 (29.2)			
Chi square test						

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 DISCUSSION

5.1.1 BIOCHEMICAL PARAMETERS DISTRIBUTION

In our study, both Continuous Ambulatory Peritoneal Dialysis (CAPD) and Hemodialysis (HD) group had similar proportion of patients with corrected serum calcium-phosphate product less than 4.5 $mmol^2/L^2$, which was 80.5% for CAPD group and 82.2% for HD group. Other study also supported this result. Lesley A.S et.al, (2003) reported that CAPD group was 71.6% and HD was 69.8% that achieved corrected serum calcium phosphate product.This finding was also consistent with the 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012 which the proportion was 71% for CAPD group and 72% for HD group.

For the target phosphate level recommended by Kidney Disease Improving Global Outcome (KDIGO) (0.8 to 1.4 mmol/L), HD group had better phosphate control with 23.4% patients achieved the target compared with CAPD group with only 19%. However, this finding was not consistent with 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012 which stated about 27% of CAPD patients achieved target phosphate level compared to only 15% in HD patients. The other study by Lesley A.S et al, (2003) found that there was no difference between HD and CAPD group with the proportion of HD was (61.3%) and CAPD group was (60.8%) respectively. Previous study have emphasized the need for vigorous control of hyperphosphatemia to improve the survival of end-stage renal disease (ESRD) patients (Mahdia, 2006). Both CAPD and HD groups that achieved target doesn't showed

higher percentage in our study. This may be due to the variation of medication that influence the phosphate level among chronic dialysis patients nowadays.

Based on 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012, CAPD patients had relatively lower level of iPTH level compared to HD patients. Our study had found the same result as the mean of iPTH for CAPD patients was 545.72 pg/ml, while for HD was 1517.87 pg/ml. This result also supported by other research by Lasley A.S et al, which reported that HD had higher mean of intact parathyroid hormone (iPTH). Besides, other study by Yonova (2007), they found that for CAPD patients, there was lower mean level of all bone markers compare to HD patients which include intact parathyroid hormone (iPTH).

For alkaline phosphatese (ALP), we supported the above result which ALP level for HD was higher with the mean of 154.96 U/L, while the mean for CAPD was 134.84 U/L. Study by Onyemekeihia (2012) had agreed that elevated serum alkaline phosphatase presence in the histological evidence of renal osteodystrophy.

From the results, HD showed the highest level of intact parathyroid hormone (iPTH) and alkaline phosphatase (ALP). Our HD patients mostly were dialysed for more than 5 years which meant that they were being dialysed adequately. One of the contributing factors if the elevation of serum iPTH and ALP was dialysis duration and it meant that the prevalence may even be higher if our patients are dialysed in a long-time period (Onyemekeihia, 2012).

5.1.2 MEDICATION DISTRIBUTION

There were no major changes in phosphate binders usage trend among CAPD and HD patients. Calcium carbonate remained as main phosphate binder since 1997 (MDTR, 2012). Majority of the patients in our study with 90.8% of CAPD patients and 91.6% of HD patients also used calcium carbonate, while the remainder mostly used Non Calcium carbonate binder i.e Lanthanum. 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012 also mentioned that majority of Sevelamer usage came from NGO sectors but for lanthanum, about 40% of usage was from public sector, another 30% were from NGO and private sector. This result indicated that phosphate level were being concerned in order to prevent hyperphosphatemia. Study by Onyemekeihia (2012) stated that dietary phosphate restriction and phosphate binding are effective methods of control of hyperphosphatemia.

In our study, 88.5% of CAPD patients and 71% of HD patients used calcitriol (vitamin D). 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012 stated that calcitriol remained the main vitamin D used in treatment of hyperparathyroidism for both CAPD and HD patients and its usage had been rising since 1997. Previous report of 19th Report of Malaysian and Transplant Registry (MDTR) 2011 also stated that Calcitriol remained the main Vitamin D used in treatment of hyperparathyroidism for both CAPD and HD) patients which had increased since 2002. In our study, the occurence of low bone turnover disease (LBTD) was low. It showed that in the management of medication, there was no overzealous use of vitamin D that will cause oversuppression of iPTH.

5.1.3 RENAL OSTEODYSTROPHY AMONG DIALYSIS PATIENTS

Our finding showed that more HD patients suffered high bone turnover disease (HBTD) with 29% compared to CAPD with 15.5%. The result was supported by our previous discussion which stated that HD group showed higher mean of serum intact parathyroid hormone (iPTH) and alkaline phosphatase (ALP) level compared to CAPD. While the proportion of patients had low bone turnover disease (LBTD) were higher (14.9%) among CAPD group as compared to HD patients (14%). This findings were not really consistent with 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012, which reported more HD patients suffered both low bone turnover disease (LBTD) (30%) and high bone turnover disease (HBTD) (4-6%) compared to CAPD (LBTD was 3% and HBTD were 0-1%).

5.1.4 DEMOGRAPHIC FACTORS AND PATTERN OF RENAL OSTEODYSTROPHY

In our study, there are no statistically significant association between demographic factors (age, gender, ethnicity) with pattern of renal osteodystrophy despite observed differences in the proportion in each demographic factors.

For gender, in CAPD patients, more male (19%) suffered low bone turnover disease (LBTD), while more female (16%) suffered high bone turnover disease (HBTD). In HD patients, both male (14%) and female (17%) mostly suffered HBTD. CAPD result was consistent with Couttenye (1997) who found that women seem to develop HBTD whereas men seems to more frequently develop LBTD. 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012 reported that in dialysis patients, slightly more male patients had LBTD but no gender difference was noticed for HBTD. Malaysian Dialysis and Transplant Registry (MDTR) 2012 was supported our finding. The effect of sex on the prevalence of renal bone disease was not spurious despite the unequel distribution of sex between the two patterns of renal disease (Cundy, 1985).

In our study, we found that younger patients (<60 years) had more high bone turnover disease (HBTD) in both CAPD that contributed 22% and HD was 21%. Elderly patients (≥60 years) had more low bone turnover disease (LBTD) in CAPD group (12%) as cmpared to HD (9%). This findings not consistent with 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012, which reported both LBTD and HBTD were seen more in younger age group (age <60 years). Cuddy et al (1985) stated that the susceptibility of the younger age may be related to the higher rate of bone remodelling and greater requirements for vitamin D and calcium.

There were no difference in proportions between ethnicity and pattern of renal osteodystrophy. The proportion for LBTD and HBTD for both ethnic group were almost the same percentage. Regarding the association of ethnicity and pattern of renal osteodystrophy, there was lack of study regarding this topic in Malaysian, so we can not make a comparison.

5.1.5 DIALYSIS DURATION AND PATTERN OF RENAL OSTEODYSTROPHY

We found that in CAPD group, low bone turnover disease (LBTD) and high bone turnover disease (HBTD) showed the highest percentage in patients on dialysis for less than 5 years. In HD patients, LBTD and HBTD showed the higher percentage in patients on dialysis for more than 5 years. Duration of dialysis being proved to be the contributing factor of pattern of renal disease. Onyemekeihia (2012) stated that the prevalence may even be higher if the patients are dialysed adequately.

5.1.6 CO-MORBIDITY STATUS AND PATTERN OF RENAL OSTEODYSTROPHY

We found out that patients with diabetes were more likely to develop low bone turnover disease (LBTD) in CAPD group , while non-diabetes patients were more likely to develop high bone turnover disease (HBTD) in HD and CAPD groups. This finding was consistent with 20th Report of The Malaysian Dialysis and Transplant Registry (MDTR) 2012 which stated high bone turnover disease (HBTD) were seen more in non-diabetes patients compared to diabetes patients and there were greater percentage of diabetes patients had intact parathyroid hormone (iPTH) level less than 150pg/ml compared to non-diabetes for both CAPD and HD groups. Besides, other study also supported our finding which stated that Diabetes Type 1 shown a low turnover of bone with reduction in bone formation (Lesley D.H. , 2013). This might be due to decrease in bone formation by reduced in osteoblastic activity, and an increased resorption markers, perhaps related to alterations in renal function (Lesley D.H, 2013).

5.2 CONCLUSIONS

Based on our study, corrected calcium phosphate does not had obvious different between Continuous Ambulatory Peritoneal Dialysis (CAPD) and Hemodialysis (HD) group of patients. Hemodialysis (HD) had better phosphate control compared to Continuous Ambulatory Peritoneal Dialysis (CAPD).

Intact parthyroid hormone (iPTH) level of Hemodialysis (HD) patients was higher than Continuous Ambulatory Peritoneal Dialysis (CAPD), and this result was consistent with our finding that more Hemodialysis (HD) patients suffered high bone turnover disease (HBTD) while occurrence of low bone turnover disease (LBTD) appeared low. Development of low bone turnover disease (LBTD) and high boneturnover (HBTD) in Continuous Ambulatory Peritoneal Dialysis (CAPD) patients was about the same proportion.

Our statistical findings does not have any significant association between demographic factors, duration of dialysis, and co-morbidity status with pattern of renal osteodystrophy.

5.3 LIMITATIONS

Due to time constraint, this study cannot be performed on a long-term basis and therefore, might not be as perfect as study being carried out on a longer term.

In this study, there is selection bias as the sample were not representative of the whole population of Malaysia since the study was only restricted to patients in Serdang Hospital and Kajang Hospital which fulfilled the inclusion criteria only.

Our study also is subjected to information bias as secondary data was used. The quality control for primary data cannot be assured which will results in mistaking data in certain records.

Moreover, there were lacked of prior research studies on our topic especially the local study, so we have some obstacles in our discussion because we cannot find the literature review to compare with our study.

5.4 RECOMMENDATIONS

For the future study, we hope that there are some changes that can be done. Firstly, the location of the study can be more than two centres. Maybe we can add the location in every state in Malaysia, so that the result will be more representative to the whole population in Malaysia. Besides, mistakes in recording data can occur if person in charge in collecting data not doing well and maybe do some errors during that time. So, to avoid errors in data records in hospital, nurses or person in charge in collecting the primary data in every hospital should have proper training. So that there are less missing data and mistake during keep the data in the record.

From our finding, we find that the renal osteodystrophy is associate with the disturbance of mineral and bone metabolism. So, we have to increase the effort to educate and create awareness in the management of calcium, phosphate and intact parathyroid hormone (iPTH) level to avoid renal osteodystrophy disease which contributed to morbidity and motility among dialysis population. Besides, the medication like Vitamin D should be monitor in patient with low bone turn over because the uses of calcitriol causing over suppression of intact parathyroid hormone (iPTH).

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APPENDIX

Table 19: PROFORMA

Bil.	Name	Age	Gender	Ethnic	Duration of dialysis	Primary disease	Calcium	Phosphate	$CaPO_4$ product	IPTH	ALP	$CaCO_3$	Vit D
1													
2													
3													
4													
5													
6													
7													
8													
9													
10													

Table 20: Gant chart

No	Activities	2013																					
		April 2013				May 2013				June 2013				July 2013				August 2013				Sept 2013			
1	Preparation of draft proposal																						
2	Submission of draft proposal																						
3	Preparation, submission and presentation of final proposal																						
4	Preparation of ethical approval and permission letters to organizations																						
5	Data collection and analysis																						
6	Submission of data analysis and presentation																						
7	Preparation of final report and scientific article																						
8	Submission of final report and scientific article																						
9	Preparation of final presentation																						
10	Final presentation																						
11	Correction of project report																						
12	Submission of report, scientific article																						

Table 21: Research team

Supervisor	Dr T Kalaiselvam Thevandran Department of Medicine, FPSK, UPM
Co-supervisor 1	Dr Goh Bak Leong Department of Nephrology, Hospital Serdang
Co-supervisor 2	Dr Sanjiv Rampal Lekhraj Department of Orthopedic, FPSK, UPM
Leader	Noor Azira Binti Abdullah 162762
Member	Siti Nadhrah Binti Bacho 162366

Table 22: Budget planning

ITEM	**PRICE**
Photocopy Data Sheets	RM50
Articles and journals	RM 30
Proposal	RM 30
Reports	RM 50
Hardcover (2 copies)	RM 100
Total	**RM 260**

JKEUPM Ref No. : FPSK_Mei (13)56

a) Members of the JKEUPM who reviewed the documents:
   - Prof. Dr. Lim Thium Aun

b) Date of approval: 6/9/2013

Endorsed at JKEUPM Meeting on **6/9/2013**, attended by:

NAME	DESIGNATION	GENDER	TICK IF PRESENT
Prof. Dr. Norlijah Othman	Paediatrics& Dean, Faculty of Medicine and Health Sciences	Female	√
Prof. Dr Zamberi Sekawi	Medical Microbiologist & Deputy Dean of Research and Internationalization, Faculty of Medicine and Health Sciences	Male	√
Prof. Dato' Dr. Lye Munn Sann	Medical Statistician, Dept of Community Health, Faculty of Medicine and Health Sciences	Male	
Prof. Dr. Tengku AizanAbd Hamid	Gerontologist & Director, Institute of Gerontology	Female	√
Prof. Dr. Lekhraj Rampal	Medical Statistician, Dept of Community Health, Faculty of Medicine and Health Sciences	Male	√
Prof. Dr. Elizabeth George	Pathologist, Dept of Pathology, Faculty of Medicine and Health Sciences	Female	√
Prof. Dr. Lim ThiamAun	Anesthesiologist, Dept of Surgery, Faculty of Medicine and Health Sciences	Male	√
Prof. Dr. Wan Omar Abdullah	Medical Parasitologist, Dept of Medical Microbiology and Parasitology, Faculty of Medicine and Health Sciences	Male	
Prof. Dr. Patimah Ismail	Professor of Biomedicine, Dept of Biomedical Sciences, Faculty of Medicine and Health Sciences	Female	√
Assoc. Prof. Dr. Johnson Stanslas	Pharmacologist, Dept of Medicine, Faculty of Medicine and Health Sciences	Male	√
Assoc. Prof Dr. Mansor Abu Talib	Assoc. Professor of Guidance and Counselling, Dept of Human Development and Family Studies, Faculty of Human Ecology	Male	
Assoc. Prof. Dr. Noritah Omar (Lay Person)	Assoc. Professor of English Language, Dept of English Language, Faculty of Communication and Modern Languages	Female	
Dr. Rojanah Kahar (Lay Person)	Lecturer of Dept of Human Development and Family Studies, Faculty of Human Ecology	Female	√
Tan Sri Dato' Napsiah Omar (Independent Member)	Chairman, National Population and Family Development Board	Female	