Chapter 8: Calcium, Phosphate and Parathyroid Hormone

Overview of presentation

In the following section the figures use a common modified box-plot format with data presented separately for haemodialysis and peritoneal dialysis. The figures showing the percentage of patients reaching the Renal Association Standard include the 95% confidence interval calculated for this figure. Where medians are displayed, the 25th and 75th centiles for the unit are included. Figures showing the percentage within a range (as defined by the Renal Association Standard or a Renal Registry defined range) also include the 95% confidence interval calculated for this figure. Data completeness is indicated by the "percentage missing" figure below the unit code letter.

Harmonisation of laboratory data between hospitals

In 1998 the Renal Registry joined with the Association of Clinical Biochemists (ACB) to investigate methods to compare laboratory results between hospitals.

With the use of local reference ranges, the result for a sample analysed in one laboratory using one analytical method may differ significantly from that generated by another laboratory using another method. For many analytes, the local laboratory reference range is mainly derived from a population distribution. For some analytes (e.g. iPTH), this may be variably derived from a reference textbook, or the manufacturer's kit specification (which would be derived from a US population distribution). While the laboratory data is both appropriate and valid for use within the local hospital environment it is possible that the ability of a Unit to meet the Renal Association Standard may be compromised not only by its clinical efficiency or case mix but also by the derivation of the local reference range.

Clinical Laboratories are all required to participate in national external quality assessment schemes, in which samples are distributed to all participating laboratories for analysis. The results are compiled by organisations such as UK NEQAS to evaluate the degree of agreement between methods and between laboratories. These schemes act as an objective management tool for maintaining and improving professional standards, analogous to the Registry's own aims.

On behalf of the ACB the Clinical Biochemistry laboratories contributing results to Registry linked Renal Units were approached for permission to look at their External Quality Assessment data, access to which is only given if permission is granted. This resulted in harmonisation factors being produced from UKNEQAS. Where the Renal Standards document specifies a range of values for a standard, harmonisation is achieved by using an adjustment for that laboratory from UKNEQAS, against the all laboratory mean for that method held by UKNEQAS. Where the Renal Standards document specifies that the local reference range should be used to define a standard, the percentage of patients achieving the standard was calculated without using the laboratory harmonisation factor produced for the Registry by UKNEQAS.

Calcium

Measurement of serum calcium

Centre	Method	Uncorrected range	Corrected range	Correction formula
A	CPC	2.20-2.60	2.20-2.60	+0.02(40-Alb)
B	Arsenazo	Not Reported	2.10-2.60	+(40-Alb)/40
C	Arsenazo	2.20-2.60	Not Reported	+0.0175x(40-ALb)
D	CPC	2.10-2.65	Not Reported	+0.02(40-Alb)
E	CPC	2.05- 2.60	2.05- 2.60	+0.025(40-Alb)
F	Electrode	2.13-2.63	Not Reported	+0.02(40-Alb)
G	CPC	2.20-2.60	Not Reported	+0.02(40-Alb)
H	Arsenazo	2.20-2.63	Not Reported	+0.025(40-Alb)
I	Arsenazo	2.10-2.60	2.10-2.60	+0.02(40-Alb)
J	Arsenazo	2.22-2.58	2.22-2.58	+0.0116(40.1-Alb)
K	CPC	2.20-2.60	2.20-2.60	+0.016(46-Alb)
L	CPC	2.12-2.65	Not Reported	Not Reported
M	Arsenazo	2.12-2.62	Not Reported	Not Reported
N	CPC	2.12-2.55	2.12-2.55	+0.025(40-Alb)
O	Arsenazo	2.10-2.60	Not Reported	+0.02(40-Alb)
P	Arsenazo	2.20-2.60	Not Reported	Not Reported
Q	CPC	2.20-2.60	2.20-2.60	+0.017(43-Alb)
R	Electrode	2.20-2.60	2.20-2.60	+(-0.016 xAlb)+0.59
T	Arsenazo	2.20-2.62	2.20-2.62	+0.02(40-Alb)

Conversion factor for calcium mg/dl = mmol/L x 4

Table 8.1 Laboratory methodologies for serum calcium

There are many different formulae to calculate total calcium, taking the measured value and correcting for serum albumin. The specific formula used varies from site to site (table 8.1). For comparison it is important that the same formula is used for all centres. Wherever possible the Renal Registry has collected the calcium data from centres uncorrected for albumin and then applied the same correction formula throughout. Some laboratories only supply corrected calcium values to the renal units and for these centres the corrected calcium was taken and a derived uncorrected value was calculated using the locally used formula supplied by each centre, in conjunction with the albumin (non-laboratory harmonised) measured.

The Renal Registry has applied a standard formula to all the calcium data of :-

$$\text{Corrected calcium} = \text{uncorrected calcium} + ((40 - \text{albumin}) \times 0.02)$$

The correction formula applies a laboratory harmonisation value to both the uncorrected calcium and the albumin.

The value for corrected calcium is therefore dependent on the local method for measuring albumin. Centre Q and J use the BCP method for measuring albumin, and this reads 2-5 g/L lower than the other sites using the BCG method. Corrected calcium values for this site will therefore be slightly high, rendering comparison with other centres invalid.

A range of 2.25 – 2.65 mmol/L was defined by the Registry for corrected calcium, as locally defined normal ranges are no longer applicable after the Registry correction. Because of all these variations, a chi-squared test for significance was not performed.

The Renal Standards document recommends that ***total calcium should fall within the normal range quoted by the local pathology laboratory, corrected for serum albumin concentration.***

Haemodialysis

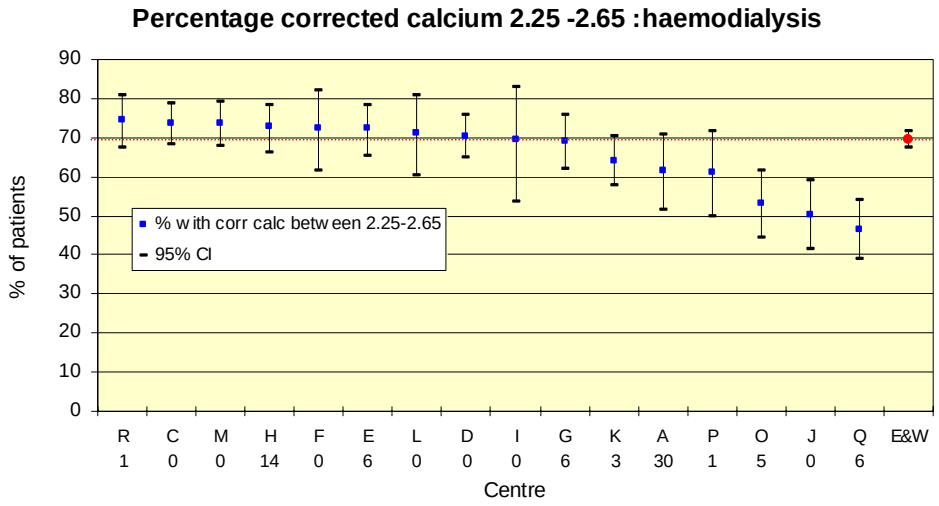

Figure 8.1 Percentage corrected calcium within 2.25-2.65 mmol/L on haemodialysis

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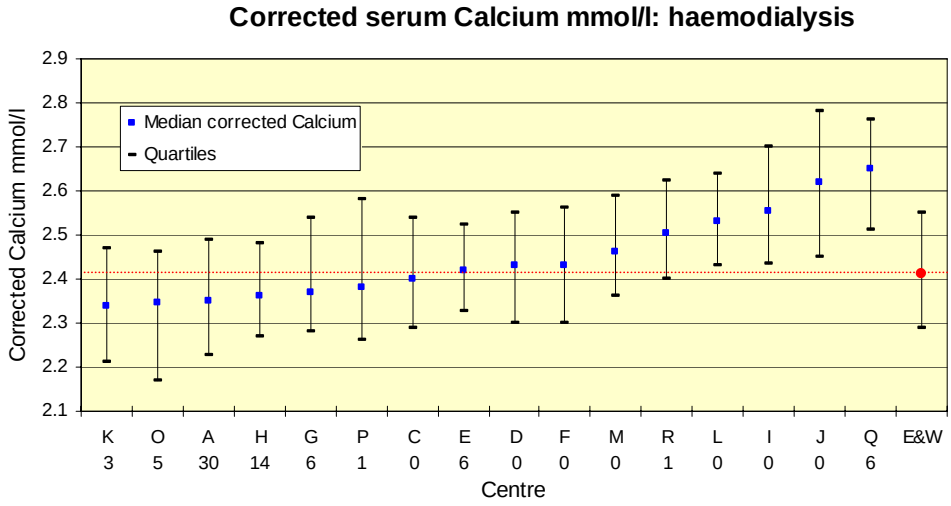


Figure 8.2 Median corrected calcium on haemodialysis

In figures 8.2 and 8.4, Centres J and Q (both use the BCP albumin method) have very high median corrected serum calcium on both haemodialysis and peritoneal dialysis. The differences are less marked in figures 8.5 and 8.6 when using the uncorrected values. This may indicate that albumin correction may be inadequate for centres using the BCP method to measure albumin.

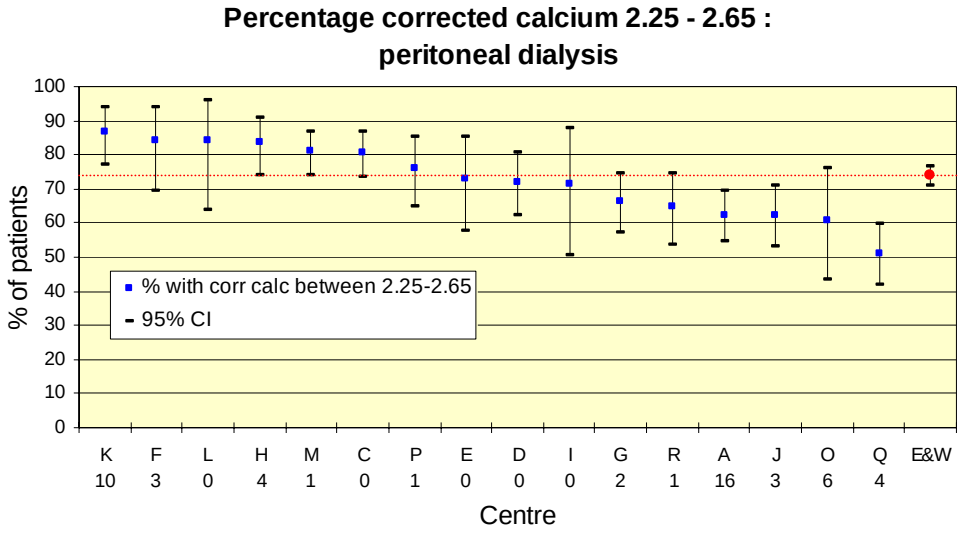


Figure 8.3 Percentage corrected calcium in range 2.25-2.65 mmol/L on peritoneal dialysis

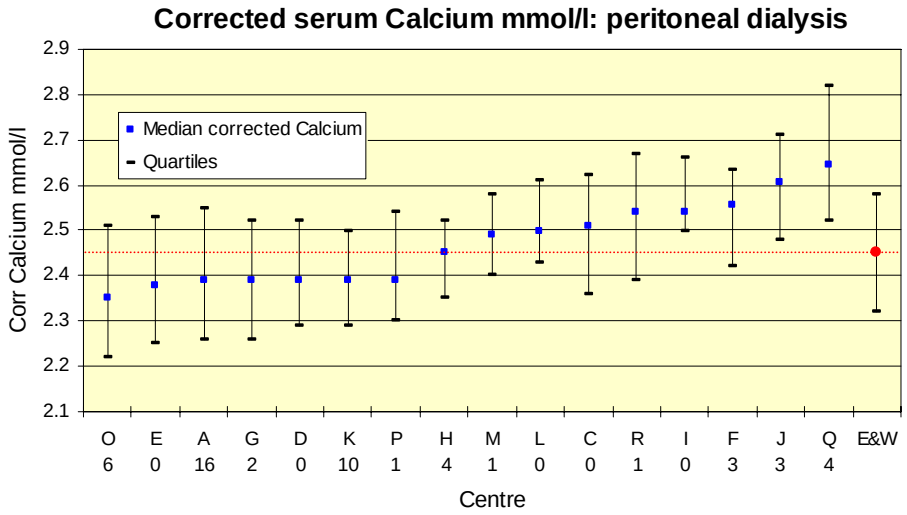


Figure 8.4 Median corrected calcium on peritoneal dialysis

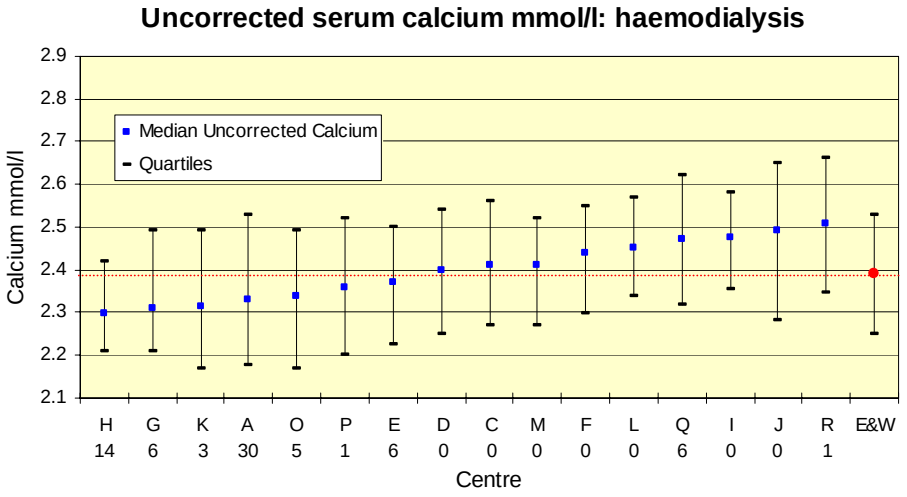


Figure 8.5 Median uncorrected serum calcium on haemodialysis

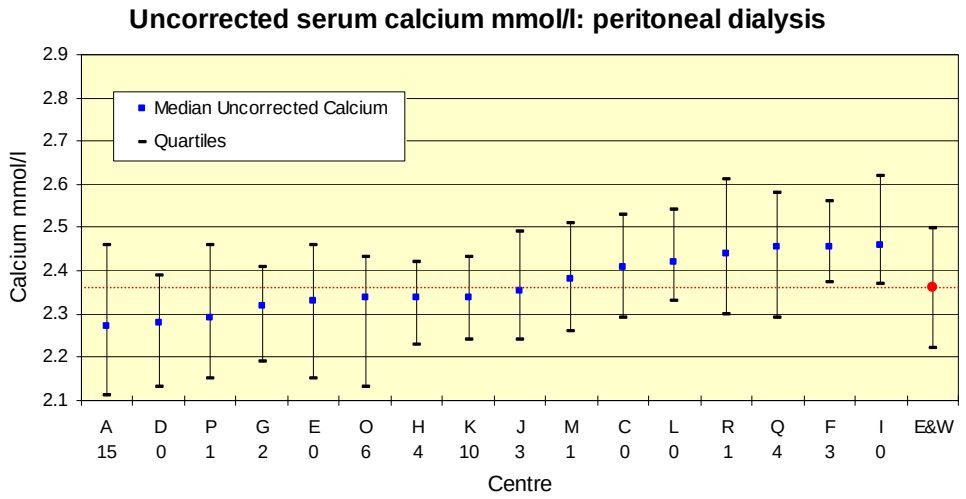


Figure 8.6 Median uncorrected serum calcium on peritoneal dialysis

Phosphate

An analysis of serum phosphate and outcome is included at the end of this chapter.

Measurement of phosphate

Centre	Methodology	Lab reference Range mmol/L	harmonisation factor (multiplier)	Derivation of ref Range
A	PMb	0.80-1.40	0.964	Manufacturer
B	PMb	0.80-1.40	0.996	Local
C	Fish/Sub	0.80-1.40	Not available	Not available
D	PMb	0.75-1.35	0.954	Not available
E	PMb	0.80-1.45	0.984	Text book
F	PMb	0.82-1.55	Not available	Text book
G	PMb	0.80-1.45	1.024	Local
H	Fish/Sub	0.75-1.36	1.011	Manufacturer
I	PMb	0.90-1.50	1.011	Local
J	PMb	0.75-1.40	1.003	Local
K	PMb	0.80-1.30	1.007	Local
L	PMb	0.80-1.40	Not available	Not available
M	PMb	0.80-1.45	0.960	Local
N	PMb	0.80-1.40	1.009	Manufacturer
O	PMb	0.74-1.40	0.971	Local
P	Fish/Sub	0.80-1.40		Local
Q	PMb	0.80-1.40	1.010	Local
R	PMb	0.70-1.40		Local
T	PMb	0.80-1.45		Text book

Conversion factor mg/dl = mmol/L x 3.1

Table 8.2 Phosphate methodologies

The comparative phosphate data is laboratory harmonised where available. There is variation of the upper reference range from 1.30 to 1.55 mmol/L (table 8.2). This variation in range does not correlate with UKNEQAS harmonisation factors that have been applied and does not appear to be related to the achievement of the Standard.

Haemodialysis

The Renal Standards document recommends ***a target range for predialysis serum phosphate of 1.2 –1.7 mmol/L.***

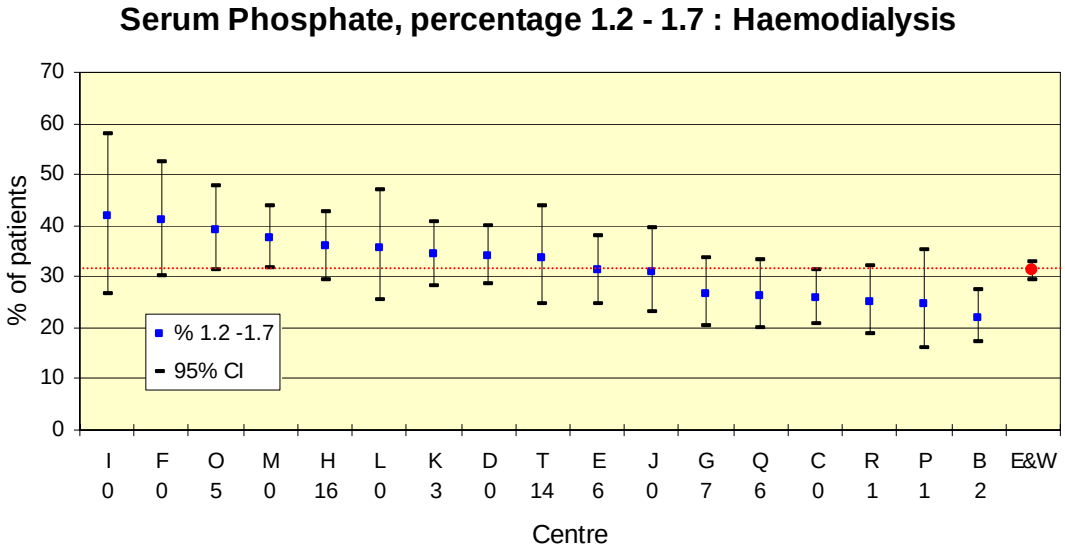


Figure 8.7 % patients with serum phosphate between 1.2 and 1.7 mmol/L on haemodialysis

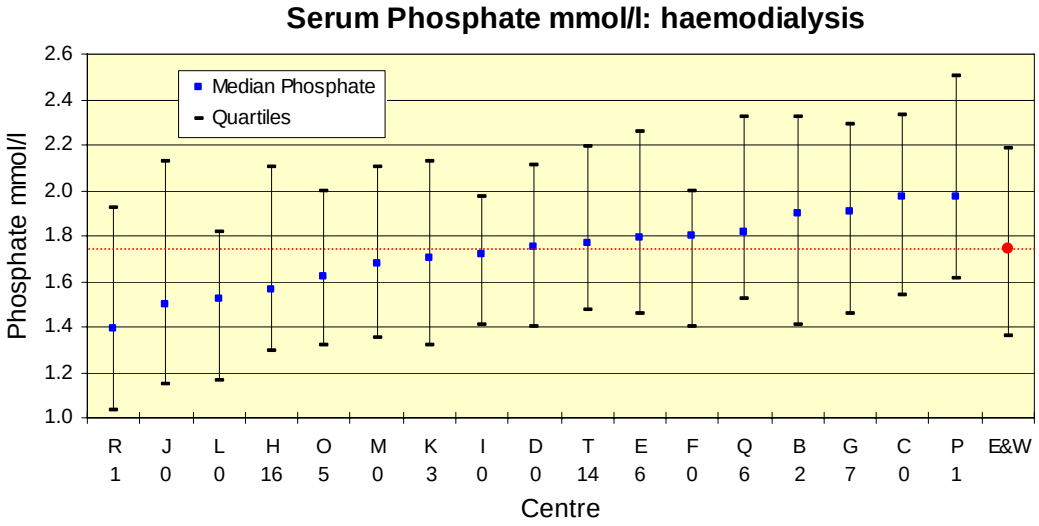


Figure 8.8 Median serum phosphate on haemodialysis

A chi-squared test was used to determine whether the percentage of patients on haemodialysis with phosphate ≤ 1.70 differed between centres. For these patients the percentage with phosphate ≤ 1.70 differed significantly between centres (X^2 = 100.7, d.f. = 16, p<0.001).

Only 31% (95% C.I. 29-33%) of serum phosphates are within the Standard and achievement of the Standard ranged from 22% to 42%. The Standard for phosphate is clearly very difficult to achieve, although centres may be influenced by the recent USA study which indicates that mortality is only increased for serum phosphate >2.1 mmol/L (Block et al).

Peritoneal dialysis

The Renal Standards document recommends ***a target range for serum phosphate of 1.1 –1.6 mmol/L.***

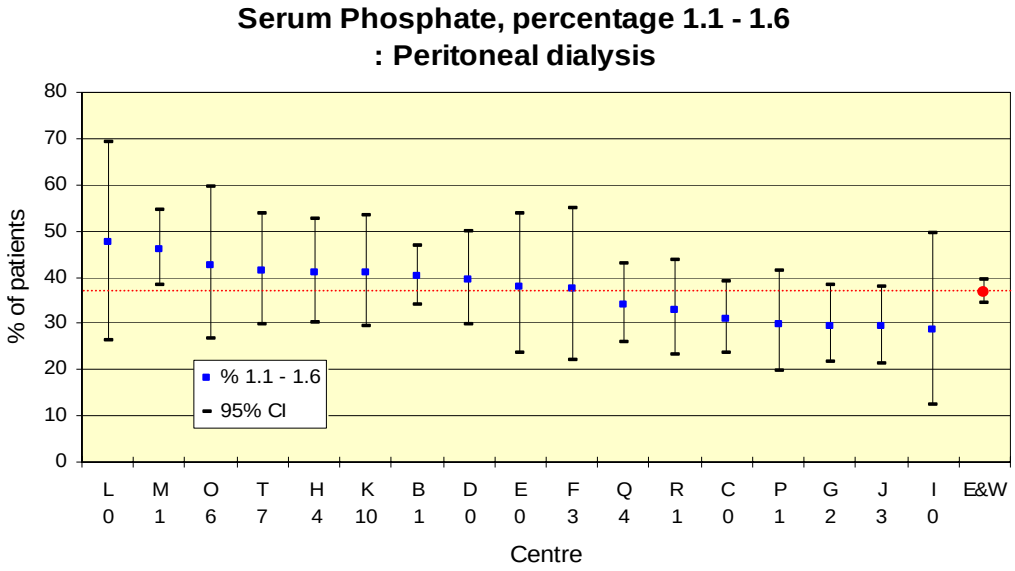


Figure 8.9 % patients with serum phosphate between 1.1 and 1.6 mmol/L on peritoneal dialysis

A chi-squared test was used to determine whether the percentage of patients on peritoneal dialysis with phosphate ≤ 1.60 differed between centres. For these patients, the percentage of patients with phosphate ≤ 1.60 differed significantly between centres ($X^2 = 34.4$, d.f. = 16, p=0.005).

Achievement of the Standard in peritoneal dialysis patients ranges from 29% to 49% with even greater overlap of the 95% confidence interval (caused by smaller numbers of patients) than in haemodialysis patients. The overall achievement of the Standard for England and Wales is 37%.

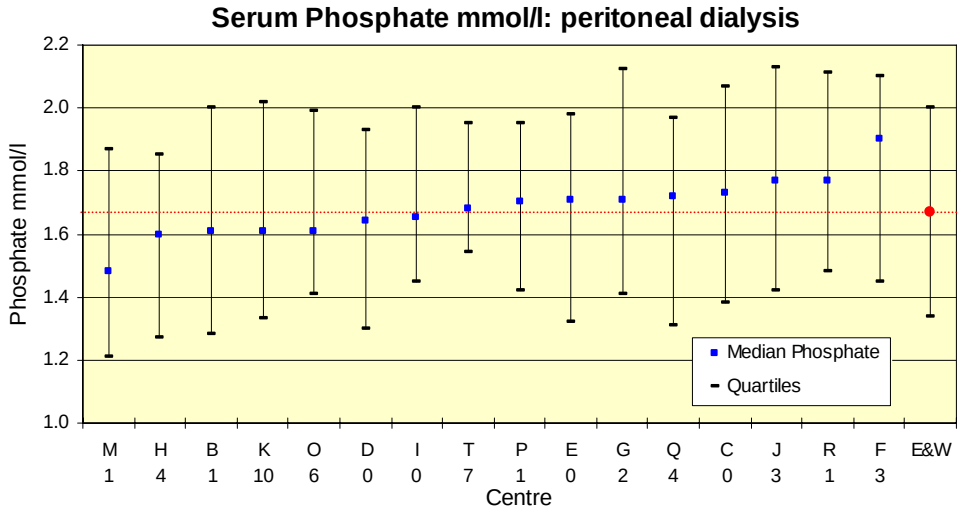


Figure 8.10 Median serum phosphate on peritoneal dialysis

Changes in serum phosphate 1997 – 1998

The changes in serum phosphate have been analysed over a two year period for the nine renal unit with data available for 1997 and 1998. The three time points displayed are 1st quarter 1997, 1st quarter 1998, 4th quarter 1998.

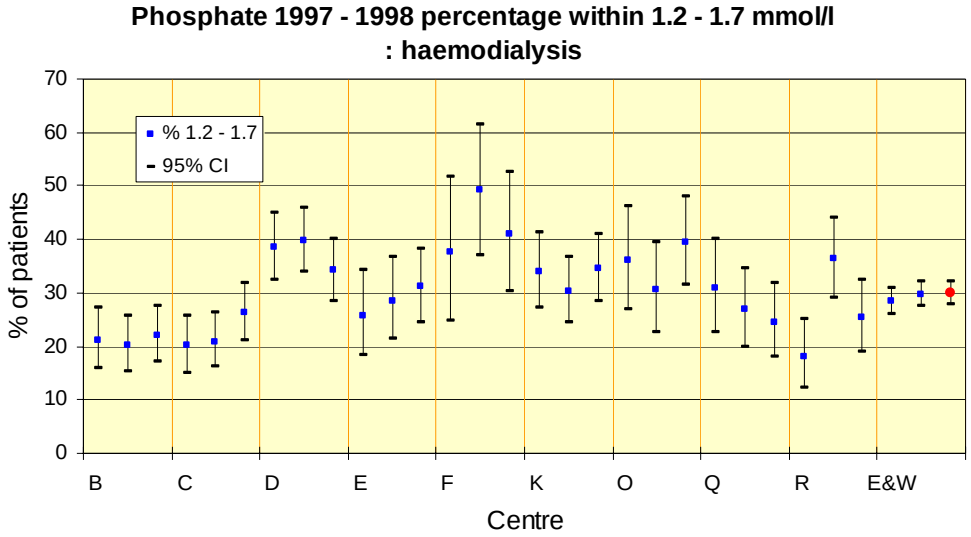


Figure 8.11 Change in % phosphate 1997 – 1998 in range 1.2-1.7 mmol/L on HD

Figure 8.12 shows the proportion of patients at these time points with serum phosphate concentration banded into 3 ranges above the upper limit of the Standard. Although centre B shows little change in compliance wihin the Standard, there has been a consistent decrease in the percentage of patients with serum phosphate above 1.7, especially in the 2.1 - 2.9 mmol/L range. This must have therefore been accompanied by an increase in patients with low serum phosphate.

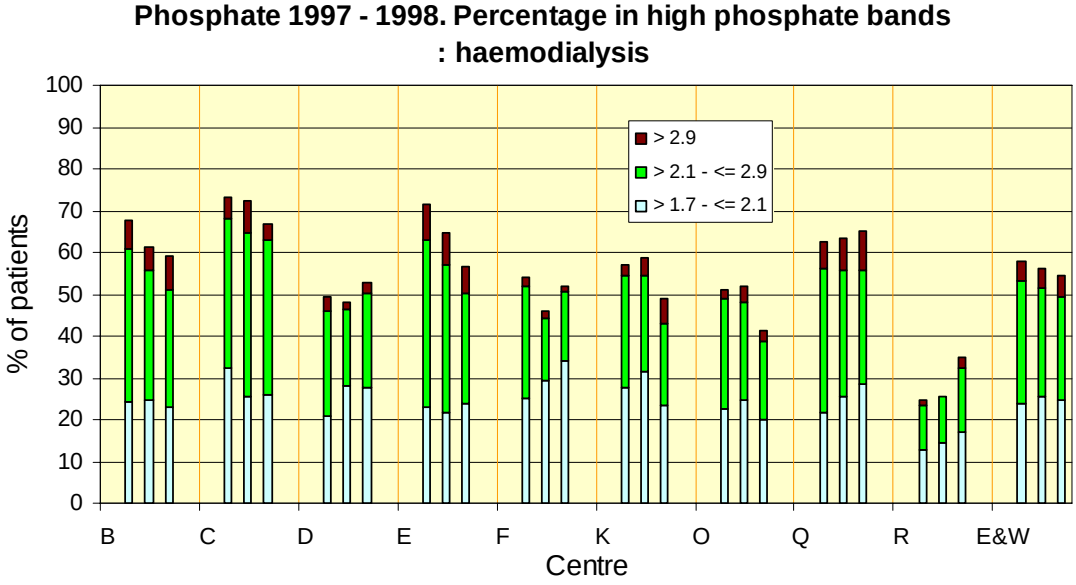


Figure 8.12 Change 1997-1998 of percentage in high phosphate bands on HD

Centre E shows a reduction in the higher serum phosphate levels but with an overall increase in the number of patients within the Standard. Within 1998 centre K and O also appear to show a reduction in patients with high serum phosphate. The reduction for centre F in the 2.1-2.9 mmol/L band is matched by an increase in the lower 1.7 –2.1 band.

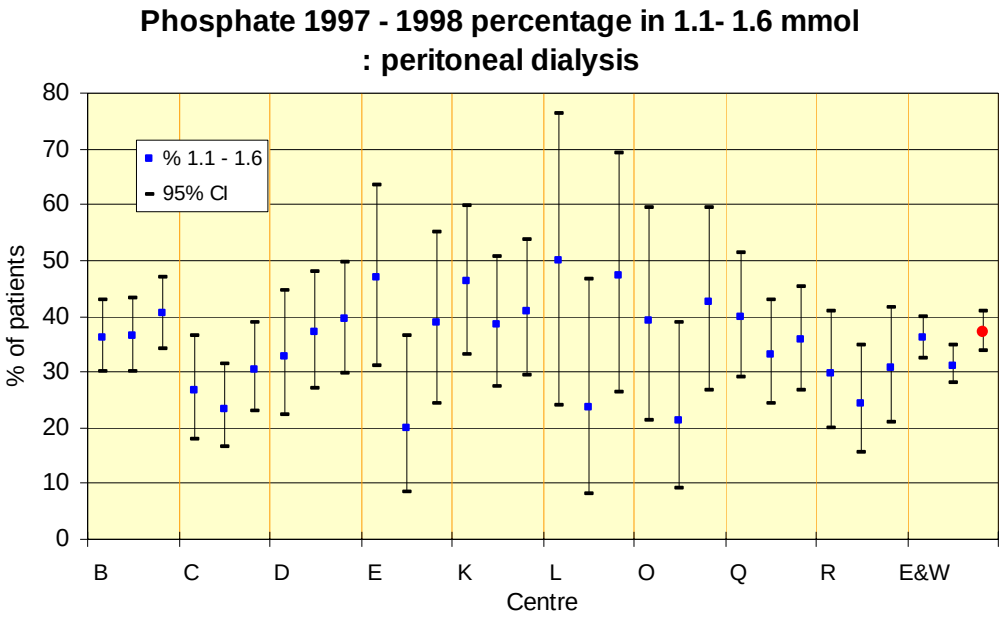


Figure 8.13 Change in phosphate 1997-1998 between 1.1 and 1.6 mmol/L on PD

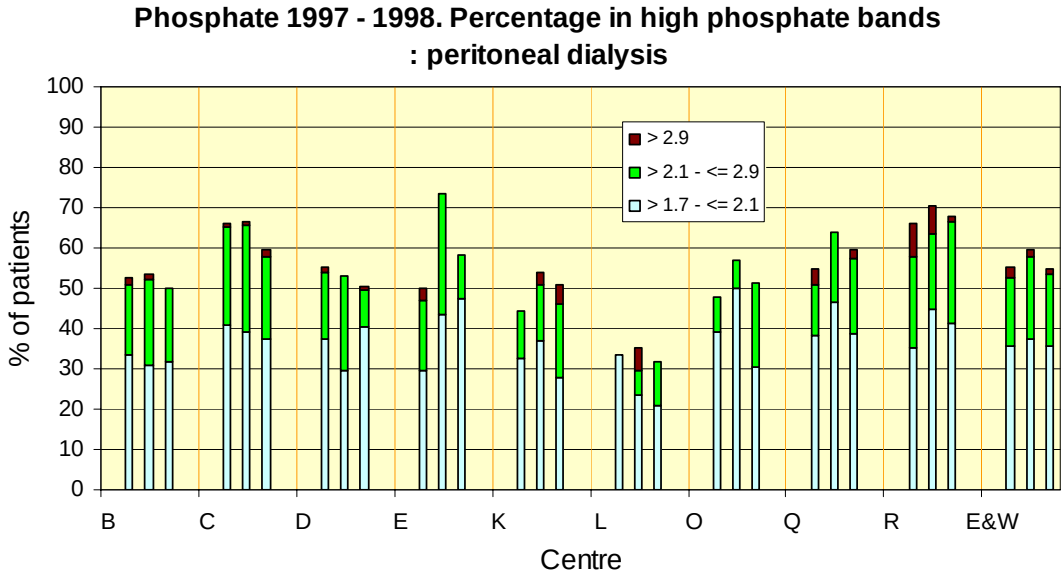


Figure 8.14 Change 1997-1998 of percentage in high phosphate bands on PD

Centre L consistently has the lowest percentage of peritoneal dialysis patients with high serum phosphate although this centre has a very small number of patients on peritoneal dialysis. The percentage of patients with phosphates above 2.1 mmol/L varied between centres from 10 – 25%. The increased compliance with the Standard for centre D is not just due to a reduction in high serum phosphate but also an increase in low serum phosphate.

Changes in serum phosphate during 1998

For 14 centres serum phosphate was available for haemodialysis patients for both the 1st quarter 1998 and the 4th quarter 1998. There were 16 centres with serum phosphate data for patients on peritoneal dialysis.

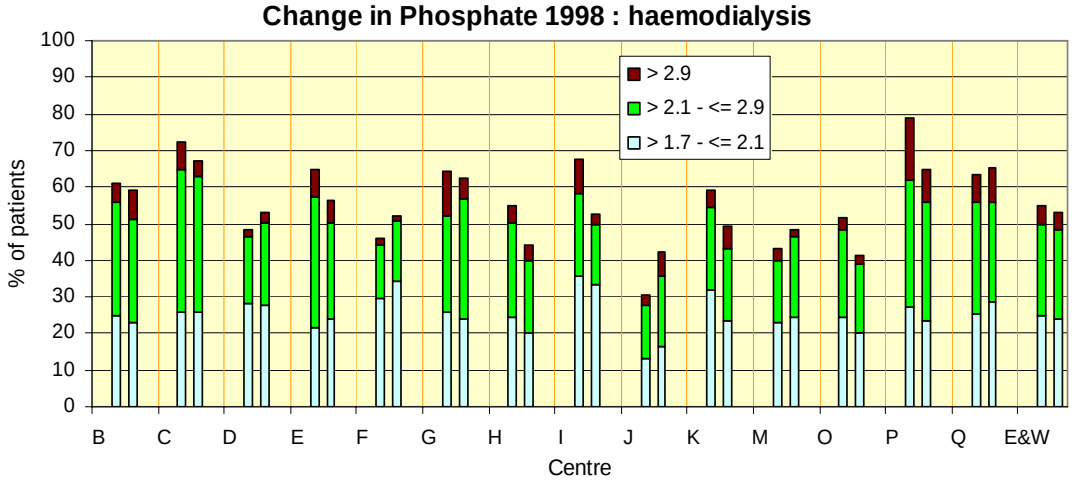


Figure 8.15 Change in phosphate in 1998 on haemodialysis

For England and Wales as a whole there has been no change in the percentage of dialysis patients with a high serum phosphate during 1998, but the time course is short.

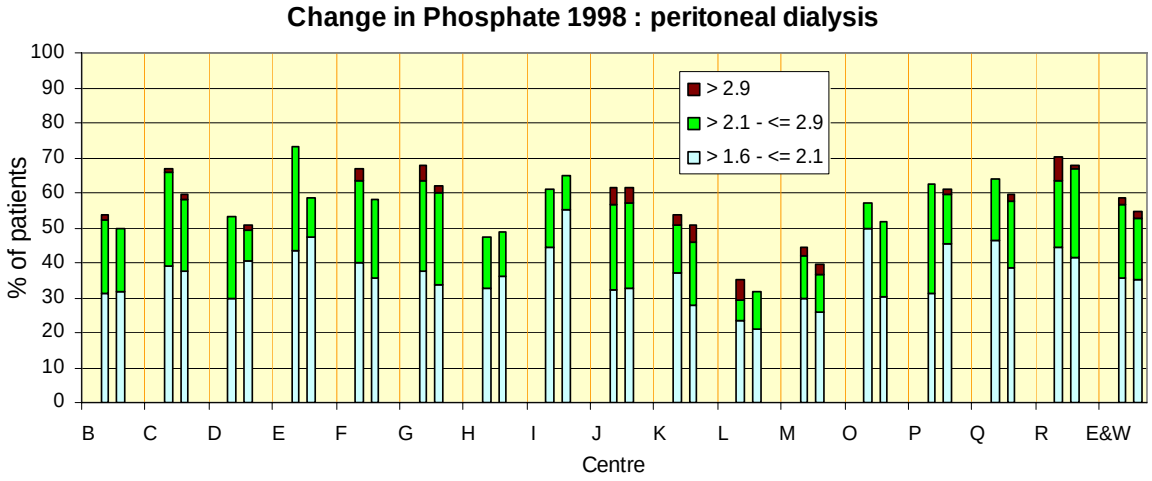


Figure 8.16 Change in phosphate in 1998 on peritoneal dialysis

Parathyroid hormone

Parathyroid hormone is defined as missing if it has not been measured within the previous 9 months.

The Renal Standards document recommends ***that iPTH (intact hormone assay) should be maintained at between 2 and 3 times the local normal range***

As discussed in the 1998 Report, the local reference range is variable even between laboratories using the same methodology (table 8.3.). This gives a variation in the upper limit for the Standard varying between 12 – 22.8 pmol/L. For comparative purposes the Registry has used the most widely quoted upper limit of 22.8 pmol/L., but acknowledges that there is no other specific reason for preferring this value.

Centre	Methodology	Lab ref Range	3 x upper ref. Range	Derivation of ref Range
A	DPC	0.9 – 6.8 pmol/L	20.4	
B	DPC	0.9 - 5.4 pmol/L	16.2	
C	Chiron	0.9 – 6.8 pmol/L	20.4	Manufacturer
D	Chiron	< 4.0 pmol/L	12.0	Local
E	DPC	1.3 – 7.6 pmol/L	22.8	Manufacturer
F	Chiron	0.8 -5.4 pmol/L	16.2	Manufacturer
G	Chiron	0.8 - 5.4 pmol/L	16.2	Manufacturer
H	INCSTAR/DPC	0.9 – 6.5 pmol/L	19.5	Manufacturer
I	Nichols	0.9 – 6.8 pmol/L	20.4	Manufacturer
J	DPC	1.3 – 7.6 pmol/L	22.8	Manufacturer
K	Nichols	0.9 – 6.8 pmol/L	20.4	Manufacturer
L	DPC	1.3 - 7.6 pmol/L	22.8	Manufacturer
M	Nichols	1.0 - 6.1 pmol/L	18.3	
N	DPC	1.3 – 7.6 pmol/L	22.8	Manufacturer
O	DPC	1.3 – 7.6 pmol/L	22.8	Manufacturer
P	DPC	1.3 - 7.6 pmol/L	22.8	Manufacturer
Q	DPC	1.3 – 7.6 pmol/L	22.8	Manufacturer
R	DPC	1.3 – 7.6 pmol/L	22.8	Manufacturer
T	INCSTAR	0.8 - 4.8 pmol/L	14.4	Manufacturer

conversion factor ng/L = pmol/L x 9.5

Table 8.3 Laboratory methodology for serum iPTH

Centre H has changed its methodology within the year form DPC to Incstar. Data is not shown for this centre as more than 50% was missing.

Haemodialysis

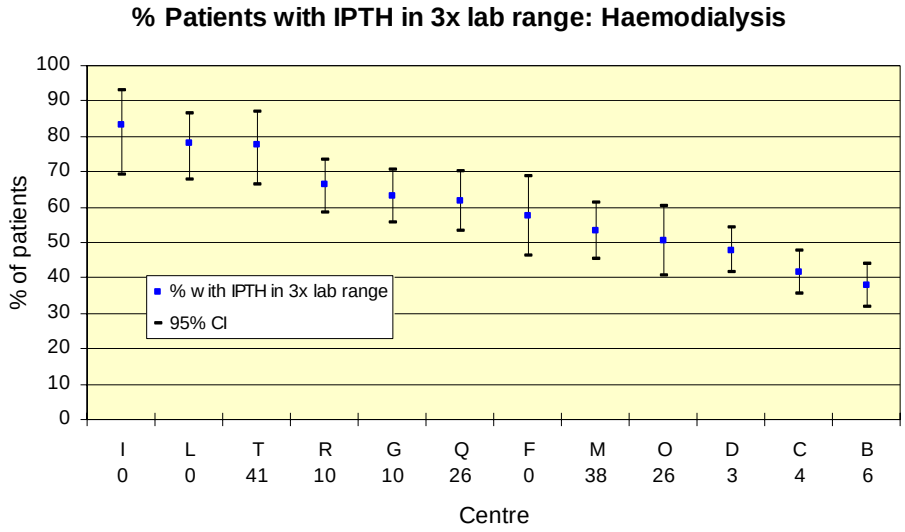


Figure 8.17 Percentage patients with iPTH in 3x lab range on haemodialysis

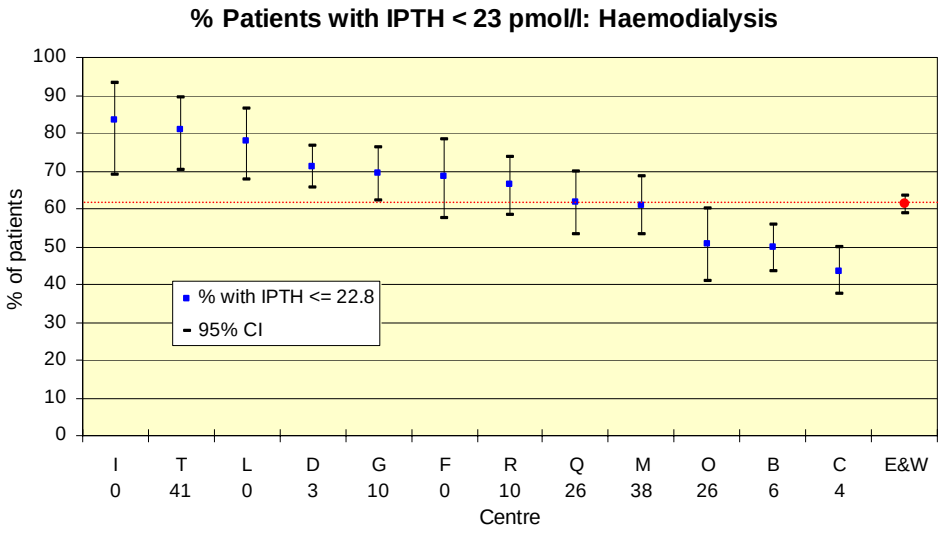


Figure 8.18 Percentage patients with iPTH < 23 pmol/L on haemodialysis

A chi-squared test was used to determine whether the percentage of patients with laboratory harmonised iPTH ≤ 22.8 differed between centres. For patients on haemodialysis, the percentage of patients with iPTH ≤ 22.8 differed significantly between centres ($X^2 = 96.7$, d.f. = 11, $p<0.001$).

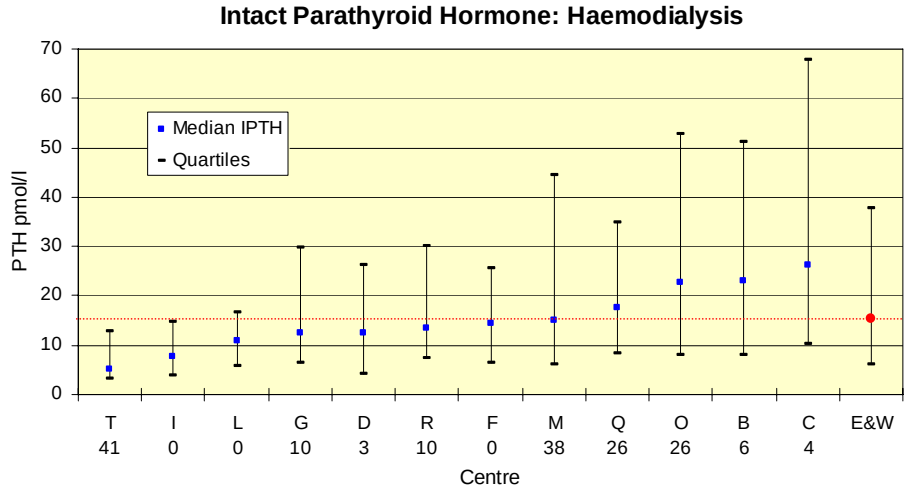


Figure 8.19 Median intact parathyroid hormone on haemodialysis

The variation in approach is more clearly seen by looking at the quartile range. For centre I 50% of patients have iPTH between 4 – 15 pmol/L while at centre C 50% are between 10 – 68 pmol/L.

Peritoneal dialysis

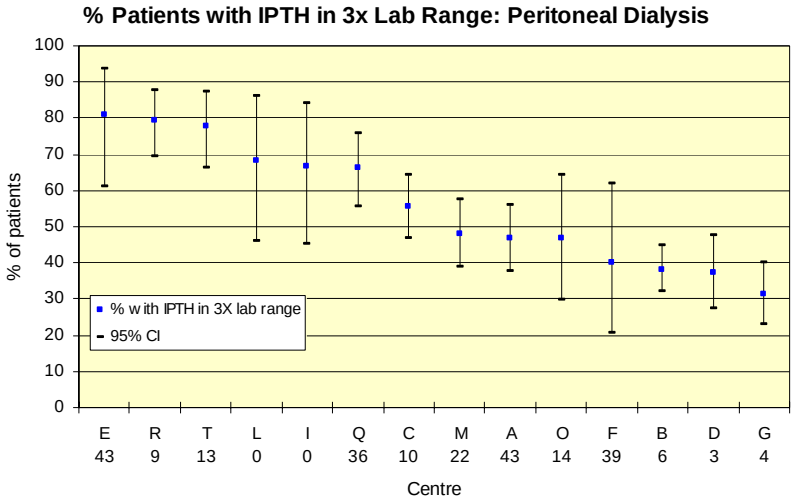


Figure 8.20 Percentage patients with iPTH in 3x lab range on peritoneal dialysis

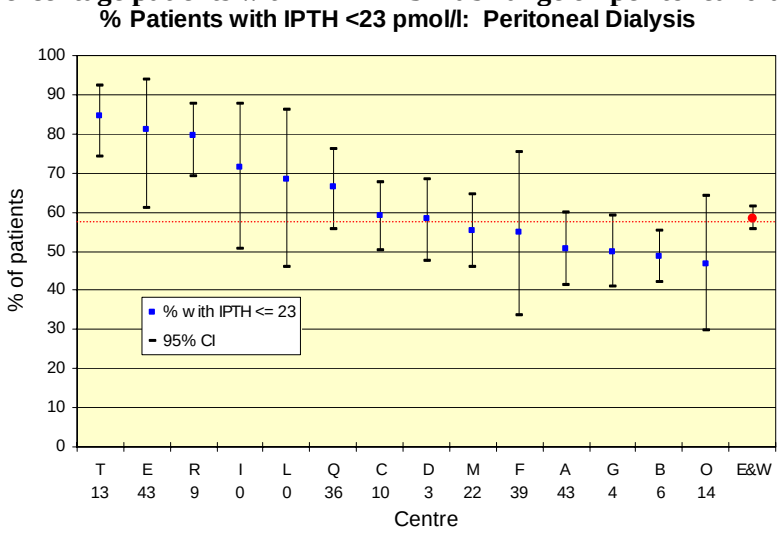


Figure 8.21 Percentage patients with iPTH < 23 pmol/L on peritoneal dialysis

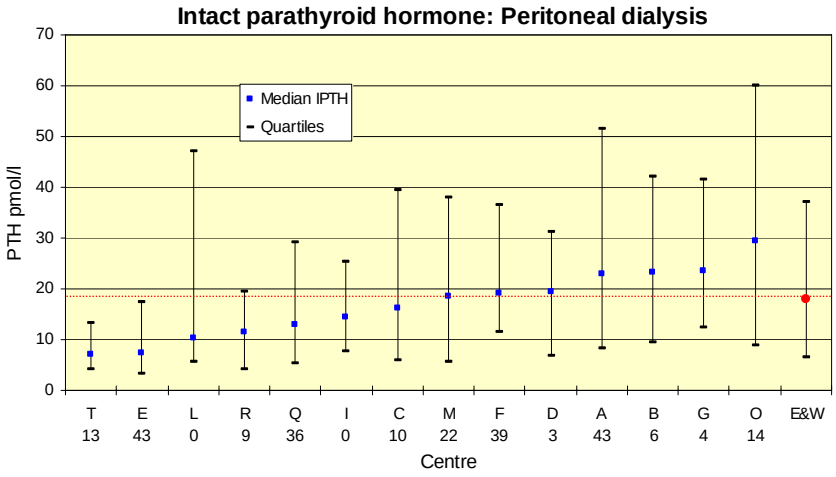


Figure 8.22 Median intact parathyroid hormone on peritoneal dialysis

For patients on peritoneal dialysis, the percentage of patients with iPTH ≤ 22.8 differed statistically significantly between centres ($X^2 = 55.9$, d.f. = 13, $p<0.001$).

At least one centre has a policy of only measuring iPTH when there are other indicators of hyperparathyroidism. This might cause a bias in the results, with a high proportion of iPTH levels being recorded from these centres. However there was no correlation between the percentage of missing data and compliance with the Standard.

Conclusions

1. Algorithms used to correct serum calcium concentration for serum albumin concentration measured may not be appropriate when BCP methods are used to measure serum albumin.

2. All Centres had difficulty reducing high serum phosphates. Many centres may feel that the Renal Association Standard for serum phosphate is unachievable and has little evidence based justification. Using the best current evidence some Centres may only be trying to control serum phosphate to below 2.1 mmol/L.

3. There has been no change over 2 years in the percentage of haemodialysis patients with high serum phosphate.

4. Figures showing compliance with a Standard (e.g. for serum phosphate) may mask change if the whole population shifts so that although more patients in the upper limit have moved into range, patients may drop below the lower limit.

5. There are varying practices between centres in the management of secondary hyperparathyroidism and many centres have a high proportion of missing data.

Serum Phosphate and Mortality

Introduction

In 1997 there were 11 centres on the Registry. This analysis relates serum phosphate of patients in 1997 to their risk of death through 1998.

Lowrie et al in 1990 reported a relationship between serum phosphate and mortality using data from 1987-88 from the National Medical Care database. Block et al confirmed this in 1998 using data collected from the 1990 Case Mix Adequacy Study and 1993 Dialysis Morbidity and Mortality Study.

Since the data for the above studies were collected there has been a general move in the USA and the UK towards improved dialysis clearance. This may have reduced the average serum phosphate of prevalent patients, and could have altered the relationship between serum phosphate and mortality. To investigate this the Registry compared distribution of serum phosphates from two centres in the UK for the years 1990, 1993, and 1997.

Sample population

Patients who were on dialysis on 1/1/1998, at one of the 11 centres on the Renal Registry database with quarterly data for 1997 were included. Patients on renal

replacement therapy for less than a year on the 1/1/1998 were excluded from the analysis. Patients were included in the analysis, regardless of their previous renal replacement therapy modality.

Patients at Centres L and N on the 1/1/1998 were excluded from the analysis, as some of the serum phosphates measured in those centres were post dialysis.

The analysis excluded patients who transferred out in 1998 to a non-Renal Registry site or received a transplant in 1998. This methodology is similar to Lowrie et al.

Statistical methods

The outcome analysed was patient death in 1998. A logistic regression analysis was used to examine the association between serum phosphate and risk of death, adjusting for age, length of time on renal replacement therapy, a primary diagnosis of diabetes and the treatment centre. These methods are similar to those used by Lowrie et al. Age and length of time on renal replacement therapy were entered into the model as continuous variables. The length of time on renal replacement therapy was measured in days on the 1/1/1998 and its log transform was used in the logistic regression model. In the adjusted analysis, patients who had been on renal replacement therapy for an unknown duration and those with a primary diagnosis of 'Not sent' (as adjustment factor includes diabetes) could not be included.

The 1997 serum phosphate data were used in the analysis without being harmonised for inter-laboratory variation. Patients had differing total numbers of serum phosphate readings for 1997, ranging from 1 to 4 values. For the analysis mean serum phosphate throughout 1997, the serum phosphate from the first quarter of 1997, and the serum phosphate from the last quarter of 1997 were each related to outcome in 1998. Patients with fewer than three quarterly values of serum phosphate available were excluded.

First quarter 1997 serum phosphate was studied, as all patients in this analysis would have survived at least 9 months from this measurement. Last quarter 1997 data might include terminally ill patients who could have a higher serum phosphate from reduced dialysis prior to death or a catabolic state, or a low serum phosphate from reduced nutritional intake prior to death. These results may be predictive of death in the next quarter, but would not indicate the contribution of serum phosphate control to mid or long-term outcome.

The analysis was first carried out categorising the serum phosphate as ≤ 1.70mmol/L, 1.71 – 2.10 mmol/L and ≥ 2.11mmol/L. These ranges were chosen since ≤ 1.70mmol/L coincides with the Renal Association Standard for haemodialysis patients, and Block et al found an increased risk of death for those with a serum phosphate greater than 2.1mmol/L (6.5mg/dL). Block et al categorised the serum phosphate into quintiles. The analysis was therefore repeated using quintiles derived from UK Registry data. The quintiles used were from the mean serum phosphate throughout 1997. The ranges were: ≤ 1.47mmol/L, 1.48-1.73mmol/L, 1.74-1.96mmol/L, 1.97-2.23mmol/L and ≥ 2.24mmol/L.

The results have been described in terms of odds ratios. The reference category chosen for the first analysis was < 1.71mmol/L. For the analysis using UK Registry quintiles, the serum phosphate reference category was 1.48-1.73mmol/L.

In this context, for someone with a serum phosphate of 1.71-2.10mmol/L the odds of dying are the

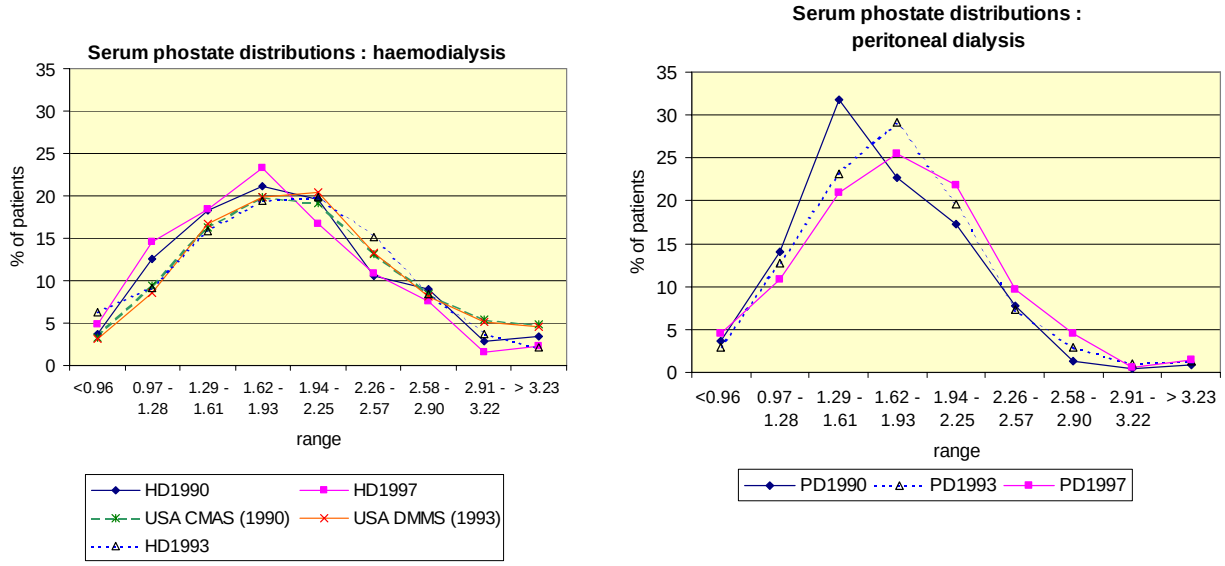
$$\frac{\text{probability of dying for someone with serum phosphate 1.71–2.10 mmol/L}}{\text{probability of surviving for someone with serum phosphate 1.7–2.10 mmol/L.}}$$

The **odds ratio** for someone with a serum phosphate of 1.71-2.10mmol/L is the odds of dying for someone with a serum phosphate of 1.71 – 2.10mmol/L divided by the odds for someone in the reference category.

Results

1. Distribution of serum phosphates 1990 – 1997

These bands were chosen to compare the published USA data.



Formula to convert from mmol/L to mg/dl is: - **mg/dl = mmol/L x 3.1**

Figure 8.23 Serum phosphate distribution by year

These results demonstrate that for patients on haemodialysis, the serum phosphates from 2 centres in the UK in 1990 and 1993 were similar to the USA data in those years. The 1997 distribution of haemodialysis serum phosphate data appears to have changed with more patients in the lower 0.97 – 1.93 bands.

For patients on peritoneal dialysis there is a shift in 1997 towards higher serum phosphates, with more patients in the 1.62 –2.90 bands.

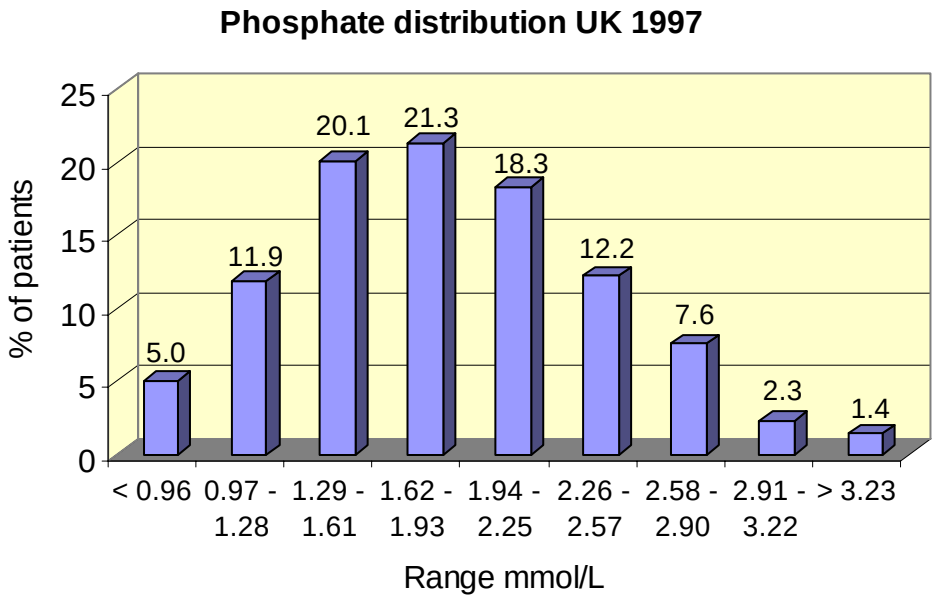


Figure 8.24 Serum phosphate distribution last quarter 1997 - all modalities

Figure 8.24 shows the serum phosphate distribution from the last quarter of 1997 for all units on the Registry. This 1997 data was used in the analysis.

2. Results using the mean serum phosphate throughout 1997

For mean serum phosphate throughout the year, the three ranges ≤ 1.70mmol/L, 1.71 – 2.10 mmol/L and ≥ 2.11mmol/L were not significantly associated with risk of death either unadjusted (n=1358, p= 0.1486) or adjusted (n = 1330 p = 0.1004)

The analysis was also repeated including patients who had a transplant in 1998 to ensure that bias did not arise from excluding possibly healthier patients. Again the effect did not reach statistical significance (p=0.1584).

Mean serum phosphate was also not significantly associated with risk of death when categorised by UK quintiles unadjusted (n=1330 p=0.6272) or adjusted (n=1330 p=0.2681)

3. Results using the serum phosphate from the fourth quarter of 1997

The fourth quarter serum phosphate when categorised as ≤ 1.70mmol/L, 1.71 – 2.10 mmol/L and ≥ 2.11mmol/L was not significantly associated with risk of death either unadjusted (n=1368, p= 0.2617) or adjusted (n = 1340 p = 0.0927)

The 4th quarter serum phosphate was also not significantly associated with risk of death when categorised by UK quintiles unadjusted (n=1368 p=0.4924) or adjusted (n=1340 p=0.1897)

4. Results using the serum phosphate from the first quarter of 1997

Phosphate from First Quarter of 1997	Unadjusted Analysis (n = 1328) O.R. [95% CI]	Adjusted Analysis (n = 1299) O.R. [95% CI]
≤ 1.70mmol/L	REF	REF
1.71 – 2.10mmol/L	0.63 [0.43 – 0.92]	0.70 [0.46 – 1.03]
≥ 2.11mmol/L	0.94 [0.67 – 1.32]	1.20 [0.84 – 1.72]
X^2	6.1	6.6
d.f.	2	2
p-value	0.0475	0.0367

Table 8.4 Results using serum phosphate from 1997 first quarter

The unadjusted analysis showed a significant **reduced** mortality for patients with serum phosphates in the 1.71 – 2.10 band compared with the reference range. This just failed to reach significance in the adjusted analysis.

In the adjusted analysis patients with serum phosphates > 2.11mmol/L had an **increased** risk of dying compared to patients with serum phosphates between 1.71 – 2.10mmol/L. The odds ratio was 1.73 [95% CI 1.13 –2.67]

The 1st quarter serum phosphate was also not significantly associated with risk of death when categorised by UK quintiles unadjusted (n=1328 p=0.1113) or adjusted (n=1299 p=0.1599).

Discussion

Since 1993, there has been a reduction in the percentage of patients on haemodialysis with very high serum phosphate. This may be due to improved dialysis adequacy, but there may also have been changes in nutritional status and use of phosphate binders in that period. There are fewer peritoneal dialysis patients in the lower serum phosphate bands. This may relate to changes in nutritional status, in the population of PD patients, or in dialysis technique. In the UK, there is now a greater proportion of dialysis patients on haemodialysis.

A logistic regression was used, as this was comparable to the analysis by Lowrie et al. A survival analysis, using Cox Proportional Hazards would enable patients who had transferred out, or been transplanted, to be included and to contribute information until they were censored. The interpretation of the results would be different since the hazard ratios obtained from Cox regression would relate to whole survival experience until the end of the follow up period, where as the odds ratios obtained by logistic regression relate to the risk of dying within a year.

Block et al. combined data from two haemodialysis patient cohorts, one studied in 1990, the other in 1993. There were a total of 6,340 patients. Using a single predialysis serum phosphate measurement from each patient they demonstrated an increase relative risk of death of 1.18 (95% C.I. 1.02-1.36, p=0.03) with serum phosphate between 2.1 – 2.59 mmol/L compared with serum phosphate of 1.4 – 1.7mmol/L. The risk increases to 1.39 (95% C.I. 1.19-1.58, p=<0.0001) with serum phosphate higher than this

The 1997 UK data suggests a relationship between serum phosphate in the first quarter of 1997 and the risk of death in 1998. There was an increased risk of death for patients with serum phosphate > 2.11 mmol/L when compared to those with serum phosphate between 1.71 –2.10 mmol/L although not when compared with serum phosphate < 1.71 mmol/L. This relationship was not significant when using serum phosphate data from the fourth quarter of 1997, which includes serum phosphate of patients who died within the next 3 months of this measurement. This may be due to the effects of terminal illness on serum phosphate. There is a suggestion that patients with serum phosphate between 1.71 – 2.10 mmol/L have a better prognosis than those with a lower serum phosphate. This elevated serum phosphate may reflect better nutritional status.

The risk of death was not significantly associated with serum phosphate for any of the other analyses. This may be due to the limited number of patients (1400) compared with the USA studies. This analysis will be repeated in next Registry report, which will include serum phosphate data from 6000 patients. The two year risk of death of the 1997 cohort will also be studied.

Conclusion

The results are very dependent upon the way in which serum phosphate is categorised and upon the summary statistic used. The Registry data is indicating a higher risk of death for patients with a serum phosphate above 2.1 mmol/L confirming the both the Lowrie and Block data. There is currently no indication that reducing serum phosphate below 1.70 mmol/L, as suggested by the Renal Association Standards document, is beneficial.

References

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2. Lowrie EG, Lew NL. 'Death Risk in Haemodialysis Patients: The Predictive Value of Commonly Measured Variables and an Evaluation of Death Rate Differences Between Facilities'. American Journal of Kidney Diseases. Vol. 15, No 5, 1990: 458-482.