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Original Research Article

Metacarpocortical Index to Predict Renal Osteodystrophy in Chronic Renal Failure Patients: A Hospital-Based Case Control Study

Kawaskar K[1], Gandhi Mohan R[2], Cherian Thomas[3], Mohan Kumar[4*]

[1]Assistant Professor, Department of Nephrology, Villupuram Medical College, Tamil Nadu, India
[2]Associate Professor, Department of Nephrology, Coimbatore Medical College Hospital, Coimbatore, Tamil Nadu, India
[3]Specialist Internist, Kanad Hospital, Al Ain, Abu Dhabi, United Arab Emirates
[4]Assistant Professor, Department of Community Medicine, KMCH Institute of Health Sciences and Research, Coimbatore, Tamil Nadu, India

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Corresponding Author: Dr. Mohan Kumar
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Abstract:

Objectives: To determine the role of metacarpocortical index (MCI) in predicting renal osteodystrophy among patients with chronic renal failure. Additionally, the association between laboratory parameters including blood urea, serum creatinine, serum calcium, serum phosphorous, serum alkaline phosphatase, serum uric acid and metacarpocortical index was determined.

Methods: This was a hospital-based case control study conducted in the outpatient department and inpatient wards of the Department of Internal Medicine, tertiary healthcare facility in south India between patients between 18 and 60 years of age, of both gender with chronic renal failure, regardless of the cause.

Results: The mean (SD) MCI among cases was 0.47 (0.09) and among controls was 0.71 (0.05) – the difference was found to be statistically significant ($p<0.05$). Among cases (n = 100), more than one third patients (39.0%) had blood urea levels less than 40 mg/dl; nearly half the patients (45.0%) had serum creatinine levels less than 1.4 mg/dl; a little more than half the patients (51.0%) had serum calcium between 7 mg/dl and 10.4 mg/dl; two third patients (67.0%) had serum phosphorus levels less than 4.5 mg/dl; two third patients (66.0%) had serum ALP levels between 60 IU/L and 100 IU/L; and more than two third patients (72.0%) had uric acid levels between 4 mg/dl to 7 mg/dl. The results of Pearson's correlation analysis showed that serum urea levels had significant negative strong correlation ($r=-0.69$; $p=0.001$); serum creatinine levels had significant negative moderate correlation ($r=-0.52$; $p=0.002$); serum calcium levels had significant positive strong correlation ($r=0.73$; $p=<0.001$); serum phosphorus levels had significant negative moderate correlation ($r=-0.51$; $p=<0.001$); serum alkaline phosphatase levels had significant negative strong correlation ($r=-0.70$; $p=<0.001$); and serum uric acid levels had significant negative moderate correlation ($r=-0.42$; $p=<0.001$) with MCI values in patients with CRF.

Conclusion: The study highlights the potential of MCI as an early indicator, aiding in the timely implementation of preventive measures to mitigate the risks associated with renal osteodystrophy.

Keywords: Renal osteodystrophy, Metacarpocortical index, Chronic renal failure, India.

Introduction

Chronic renal failure (CRF) is a prevalent renal condition characterized by various causes leading to the progressive decline in nephron number and function, often culminating in end-stage renal disease (ESRD).[1] Uraemia, a complex state indicative of dysfunction across all organ systems, manifests distinct signs and symptoms resulting from chronic renal failure.[2]

In cases of chronic renal disease, where the glomerular filtration rate (GFR) drops below 60 ml/min, approximately 75% of patients exhibit bone-related issues.[3] Renal osteodystrophy is a common occurrence in patients with chronic kidney disease (CKD), as the kidneys struggle to maintain appropriate calcium and phosphorus levels in the blood.[4, 5] Changes in bone may commence early in the disease progression, often remaining asymptomatic, earning the term "silent crippler."[6]

End-stage renal disease frequently results in abnormal bone turnover, coupling, and mineralization.[7] A decline in GFR below 60 ml/min leads to an increase in parathyroid hormone (PTH) and a decrease in 1,25 dihydroxy vitamin D levels, resulting in phosphate retention.[8] Elevated

PTH levels restore the balance between phosphate and calcium.[9] However, as GFR further decreases to 20-40 ml/min, maintaining normal calcium and phosphate homeostasis becomes challenging. With worsening uraemia, skeletal resistance to PTH intensifies, and abnormal bone histology becomes prevalent in nearly all patients. As the disease progresses, skeletal resistance to PTH becomes apparent.[10] Although PTH levels and Bone-Specific Alkaline Phosphatase (ALP) are useful in assessing bone disease, bone biopsy and histomorphometry remain the gold standard tests.[11] The use of calcium salts and calcitriol to alleviate osteomalacia by suppressing PTH has potential drawbacks, such as an increased risk of vascular calcification, cardiovascular mortality, and fractures.[12] Alternative options, including calcemic vitamin D analogs, calcimimetics, bisphosphonates, and sevelamer, can be considered for phosphate control. Improving Bone Mineral Density may involve the use of calcitriol and hormone replacement therapy (HRT). By employing a combination of modalities, including biochemical markers, histology, bone densitometry, and early intervention, the morbidity associated with CRF has seen a reduction.[13] One of the earliest radiological changes observed in CRF is the metacarpocortical index.[14]

Against this background, the objectives of the present study were to determine the role of metacarpocortical index in predicting renal osteodystrophy among patients with chronic renal failure. Additionally, the association between laboratory parameters including blood urea, serum creatinine, serum calcium, serum phosphorous, serum alkaline phosphatase, serum uric acid and metacarpocortical index was determined.

Materials and Methods

This was a hospital-based case control study conducted in the outpatient department and inpatient wards of the Department of Internal Medicine, tertiary healthcare facility in south India between January 2017 and December 2018. The study was approved by the Institute Human Ethics Committee (IHEC). The content of Participant Information Sheet (PIS) in local language was provided to the participants (and their attenders) and contents were read to them in their own language to their satisfaction.

The participants were enrolled in the study after obtaining written informed consent. The study had two groups – the case group or the study group included patients between 18 and 60 years of age, of both gender with chronic renal failure, regardless of the cause; the control group or the comparison group included individuals with no evidence of chronic renal failure or apparently healthy individuals of both gender between 18 and 50 years of age.

However, patients with acute renal failure, patients presenting with bony changes other than that of chronic renal failure, patients with rickets, history of drug intake (steroids) and patients not willing to provide informed written consent were excluded from the present study.

The study population was very specific – we resorted to purposive sampling. All accessible patients with chronic renal failure satisfying the inclusion criteria were included in the study using consecutive sampling technique. The minimum estimated sample size was 100 patients in the case group and 100 controls. We used a purpose predesigned, semi structured, pretested proforma to collect the patient sociodemographic characteristics, history, findings of general physical and clinical examination, laboratory parameters (Blood urea, serum creatinine, serum calcium, serum phosphorus, serum uric acid, serum alkaline phosphatase (ALP), serum vitamin D3), X-ray (Anteroposterior (AP) view) – right hand to visualise the 2nd metacarpal bone (used for computing the metacarpocortical index). Metacarpocortical index can predict quantitative bone changes which can be used for preventing complications of renal osteodystrophy (including fractures).

The data obtained was manually entered into Microsoft Excel, coded, and recoded. Analysis was done using Statistical Package for the Social Sciences (SPSS) v23. Descriptive analysis was presented using numbers and percentages for categorical variables and mean (standard deviation) or median (interquartile range) for continuous variables. To test for association, Chi-square test or Fisher's exact test (two sided) was used for categorical data; independent 't' test (two sided) was used for continuous data. One-way ANOVA with Tukey's post hoc test was used to compare the mean (SD) of more than two groups. To assess the correlation between study parameters, we used Pearsons's correlation coefficients. Statistical significance was considered at $p<0.05$.

Results

The present study included a total of 100 cases (patients 18 to 60 years of age with chronic renal failure, regardless of the cause) and 100 controls in accordance with the prespecified inclusion and exclusion criteria. Majority of the cases (36.0%) were more than 50 years of age, followed by 27.0% patients between 41 and 50 years of age. Similarly, majority of the controls (35.0%) were more than 50 years of age, followed by 29.0% between 41 and 50 years of age. Nearly two thirds of study participants in the case group (60.0%) and control group (62.0%) were males. The baseline characteristics

showed that the cases and controls did not vary significantly by age and gender.

Metacarpocortical index (MCI) is a easy to use, reliable method of predicting renal osteodystrophy in patients with chronic renal failure. In the present study, using X-ray right hand – AP view, metacarpocortical index was computed as, MCI = [Lateral + Medial cortical thickness at midpoint of second metacarpal]/Total thickness at midpoint of second metacarpal.(15) The mean (SD) metacarpocortical index among cases was 0.47 (0.09) and among controls was 0.71 (0.05) – the difference was found to be statistically significant ($p<0.05$).

Factors associated with metacarpocortical index: Among cases (n = 100), more than one third patients (39.0%) had blood urea levels less than 40 mg/dl; nearly half the patients (45.0%) had serum creatinine levels less than 1.4 mg/dl; a little more than half the patients (51.0%) had serum calcium between 7 mg/dl and 10.4 mg/dl; two third patients (67.0%) had serum phosphorus levels less than 4.5 mg/dl; two third patients (66.0%) had serum ALP levels between 60 IU/L and 100 IU/L; and more than two third patients (72.0%) had uric acid levels between 4 mg/dl to 7 mg/dl.

The mean (SD) metacarpocortical index was 0.67 (0.09) among patients with blood urea less than 40 mg/dl; 0.44 (0.12) among patients with blood urea values between 100 and 199; and 0.27 (0.04) among patients with blood urea more than or equal to 200 – the difference was found to be statistically significant ($p<0.05$).

Similarly, the mean (SD) metacarpocortical index was 0.65 (0.09) in patients with serum creatinine less than 1.4; 0.42 (0.02) among patients with serum creatinine between 6 to 10.9; and 0.30 (0.02) among patients with serum creatinine more than or equal to 11 mg/dl – the difference was found to be statistically significant ($p<0.05$). Metacarpocortical index values increased with increasing levels of serum calcium – 0.39 (0.08) among patients with serum calcium less than 7 mg/dl, 0.59 (0.11) among patients with serum calcium between 7 to 10.4, and 0.76 (0.09) among patients with serum calcium levels more than or equal to 10.5 mg/dl. The metacarpocortical index was significantly lower among patients with serum phosphorus values between 4.5 and 9.0 (Mean 0.46, SD 0.06), in comparison with patients having serum phosphorus values less than 4.5 (Mean 0.62, SD 0.07) ($p<0.05$). The metacarpocortical index was significantly lower among patients with serum ALP values more than 100 (Mean 0.31, SD 0.05), in comparison with patients having serum ALP values less than 60 (Mean 0.73, SD 0.06). Similarly, MCI was lower in patients with uric acid levels more than 7 mg/dl (Mean 0.32, SD 0.06), in comparison with patients having uric acid levels less than 4 mg/dl (Mean 0.61, SD 0.05) – a statistically significant difference ($p<0.05$).

Correlation analysis: The results of Pearson's correlation analysis showed that serum urea levels had significant negative strong correlation ($r=-0.69$; $p=0.001$); serum creatinine levels had significant negative moderate correlation ($r=-0.52$; $p=0.002$); serum calcium levels had significant positive strong correlation ($r=0.73$; $p=<0.001$); serum phosphorus levels had significant negative moderate correlation ($r=-0.51$; $p=<0.001$); serum alkaline phosphatase levels had significant negative strong correlation ($r=-0.70$; $p=<0.001$); and serum uric acid levels had significant negative moderate correlation ($r=-0.42$; $p=<0.001$) with metacarpocortical index values in patients with chronic renal failure.

Table 1: Baseline characteristics of cases and controls

		Cases N = 100	Controls N = 100	p value
		N (%)	N (%)	
Age (in years)	Less than 20	4 (4.0)	5 (5.0)	0.548
	21 to 30	11 (11.0)	10 (10.0)	
	31 to 40	22 (22.0)	21 (21.0)	
	41 to 50	27 (27.0)	29 (29.0)	
	More than 50	36 (36.0)	35 (35.0)	
Gender	Male	60 (60.0)	62 (62.0)	0.471
	Female	40 (40.0)	38 (38.0)	
Metacarpocortical index Mean (SD)		0.47 (0.09)	0.71 (0.05)	0.014*

*Statistically significant at $p<0.05$
ALP, Alkaline phosphatase; SD, Standard deviation

Table 2: Factors associated with metacarpocortical index in patients with chronic renal failure

		Cases N = 100	Metacarpocortical index	p value
		N (%)	Mean (SD)	
Blood urea (in mg/dl)	Less than 40	39 (39.0)	0.67 (0.09)	0.002*
	40 to 99	27 (27.0)	0.52 (0.11)	
	100 to 199	29 (29.0)	0.44 (0.12)	
	≥200	5 (5.0)	0.27 (0.04)	
Serum creatinine (in mg/dl)	Less than 1.4	45 (45.0)	0.65 (0.09)	0.001*
	1.4 to 5.9	24 (24.0)	0.54 (0.08)	
	6 to 10.9	20 (20.0)	0.42 (0.02)	
	≥11	11 (11.0)	0.30 (0.02)	
Serum calcium (in mg/dl)	Less than 7	5 (5.0)	0.39 (0.08)	0.010*
	7 to <10.4	51 (51.0)	0.59 (0.11)	
	≥10.5	44 (44.0)	0.76 (0.09)	
Serum phosphorus (in mg/dl)	Less than 4.5	67 (67.0)	0.62 (0.07)	0.004*
	4.5 to 9.0	33 (33.0)	0.46 (0.06)	
Serum ALP (in IU/L)	Less than 60	5 (5.0)	0.73 (0.06)	<0.001*
	60 to 100	66 (66.0)	0.63 (0.03)	
	More than 100	29 (29.0)	0.31 (0.05)	
Uric acid (in mg/dl)	Less than 4	2 (2.0)	0.61 (0.05)	0.026*
	4 to 7	72 (72.0)	0.58 (0.07)	
	More than 7	26 (26.0)	0.32 (0.06)	

*Statistically significant at p<0.05
ALP, Alkaline phosphatase; SD, Standard deviation

Discussion

The findings of our study provide valuable insights into the utility of the Metacarpocortical Index (MCI) as a predictive tool for renal osteodystrophy in patients with chronic renal failure. The study encompassed 100 cases (patients aged 18 to 60 with chronic renal failure) and 100 controls, ensuring adherence to pre-specified inclusion and exclusion criteria. The distribution of age and gender in both the case and control groups reflected a relatively balanced representation.

The majority of cases and controls aged over 50 years, highlighting the prevalence of chronic renal failure in the elderly population.[16] Additionally, the gender distribution was comparable between the two groups, indicating that the baseline characteristics were not significantly different in terms of age and gender. Our study employed the Metacarpocortical Index (MCI) as a tool for predicting renal osteodystrophy. The results demonstrated a statistically significant difference in the mean MCI between cases (0.47 ± 0.09) and controls (0.71 ± 0.05), confirming that MCI can effectively distinguish between individuals with chronic renal failure and those without.

The observed lower MCI in cases compared to controls suggests a thinner cortical thickness at the midpoint of the second metacarpal in patients with chronic renal failure. This finding aligns with the known association between chronic renal failure and alterations in bone density, mineralization, and structure, contributing to the development of renal osteodystrophy.[17] The ability of MCI to detect these changes early on emphasizes its potential as a practical and reliable method for predicting bone complications in this patient population.[18]

The significance of our findings extends to the clinical realm. The early identification of renal osteodystrophy is crucial for implementing preventive measures and managing complications, including the risk of fractures. The ease of use and reliability of MCI make it a promising tool for routine clinical assessments in patients with chronic renal failure.

The results of our study reveal significant associations between MCI and various laboratory parameters among patients with chronic renal failure, shedding light on the potential of MCI as a valuable indicator of bone health in this population. Our findings indicate a significant inverse relationship between blood urea levels and MCI.[19] Patients with blood urea levels less than 40 mg/dl exhibited a higher mean MCI compared to those with higher levels.

This inverse correlation suggests that elevated blood urea, a marker of impaired kidney function,[20] may contribute to decreased MCI values, reflecting the impact of renal dysfunction on bone health. Similarly, a significant negative correlation was observed between serum creatinine levels and MCI. As serum creatinine levels increased, MCI values decreased. This association underscores the link between the severity of chronic renal failure, as indicated by elevated serum creatinine, and the compromised bone density reflected in lower MCI values.[21]

In contrast, serum calcium levels demonstrated a positive correlation with MCI. Higher serum calcium levels were associated with elevated MCI values, indicating a potential protective effect on bone health. This aligns with the known role of calcium in maintaining bone density and highlights the importance of managing calcium levels in patients with chronic renal failure to prevent bone complications.[22] Our study observed that lower serum phosphorus levels were linked to higher MCI values.

This finding is intriguing and suggests that decreased serum phosphorus, although common in chronic renal failure,[23] may be associated with better preservation of bone density, as reflected in a higher MCI. This association merits further exploration and consideration in the context of renal osteodystrophy. The study demonstrated a significant negative association between serum alkaline phosphatase (ALP) levels and MCI.[24] Higher ALP levels were associated with lower MCI values, suggesting a potential role of elevated ALP in indicating bone turnover and increased risk of bone complications in chronic renal failure patients. Lastly, our findings indicate a significant inverse relationship between uric acid levels and MCI.[25] Higher uric acid levels were associated with lower MCI values, emphasizing a potential role of uric acid in influencing bone health in patients with chronic renal failure.

The present study is not without limitations. Firstly, the study sample size may limit the generalizability (external validity) of the findings to broader populations. The use of purposive sampling might introduce selection bias. The study being conducted at a single tertiary healthcare facility in south India may limit the generalizability of the findings to other regions or healthcare settings with different demographics and healthcare practices. The use of exclusion criteria, such as the exclusion of patients with acute renal failure, might limit the study's applicability to a broader spectrum of renal conditions. While the study uses X-ray (AP view of the right hand) for calculating the MCI, this method may have limitations in terms of radiation exposure and may not be the most practical approach in all healthcare settings. The study may not account for all potential confounding factors that could influence the observed correlations, such as dietary habits, physical activity, or comorbid conditions.

Conclusion

In conclusion, our study has provided valuable insights into the role of the Metacarpocortical Index (MCI) as a potential predictor of renal osteodystrophy in patients with chronic renal failure. The observed significant negative correlations of MCI with serum urea and creatinine levels underscore the impact of impaired renal function on bone density, emphasizing the utility of MCI as an indicative measure in this population. Conversely, the positive correlation with serum calcium levels suggests a potential protective effect of adequate calcium levels on bone health in chronic renal failure patients. Furthermore, our findings revealed significant negative correlations between MCI and serum phosphorus, alkaline phosphatase, and uric acid levels. These correlations highlight the complexity of bone metabolism in the context of chronic renal failure, where alterations in biochemical markers are associated with changes in bone structure, as reflected by the Metacarpocortical Index.

In a clinical context, our study suggests that MCI could serve as a practical and valuable tool for healthcare professionals in assessing and managing bone complications in patients with chronic renal failure. The negative correlations observed with certain laboratory parameters highlight the potential of MCI as an early indicator, aiding in the timely implementation of preventive measures to mitigate the risks associated with renal osteodystrophy.

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