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# USE OF t-ALP IN DIAGNOSIS OF MINERAL BONE DISEASE IN CKD PATIENTS ON DIALYSIS

Physiology Research

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## ABSTRACT

In patients of Chronic Kidney Disease (CKD), bone histology is routinely employed for the precise assessment of Mineral Bone Disease (MBD). The search for reliable biochemical bone parameters has been ongoing. Estimation of t-ALP has been used as main biochemical indicator in this cross-sectional observational study on dialysis patients. Biochemical analysis of total alkaline phosphatase & intact parathormone of all cases were done using fully automated equipments. To see the association among different patterns of MBD, statistical tests like Chi-square and ANOVA were used. The statistical analysis with $\chi 2$ testing of the results revealed that MBD is significantly associated with t-ALP level. The present study does not accept the null hypothesis and suggests that there is a statistically significant association of t-ALP levels with bone mineral disease (altered parathormone levels) for CKD patients on haemodialysis.

## KEYWORDS

Alkaline Phosphatase, Chronic Kidney Disease, Haemodialysis.

## INTRODUCTION

Bone tissue undergoes regular remodeling and rebuilding in healthy adults. The kidneys have an important role in maintaining healthy bone composition [1]. Renal dysfunction leads to different types of bone disorders. The term renal osteodystrophy (ROD) has been used conventionally to describe all bone and mineral disorders in patients with CKD. However, the outdated definition of ROD does not sufficiently cover all aspects of bone and mineral changes present in CKD.

To rectify this matter, the Kidney Disease Improving Global Outcomes (KDIGO) team in 2005 renamed bone and mineral disorders (MBD) in CKD and A new terminology Chronic Kidney Disease-Mineral & Bone Disorder (CKD-MBD) was introduced, which includes a broader clinical field than ROD [2],[3]. CKD-MBD as a complex syndrome, including abnormal mineral and PTH metabolism along with altered bone structure and deformities. Many Indian as well as Western researchers widely accepted this [4],[5],[6],[7]. In patients of Chronic Kidney Disease (CKD), bone histology is routinely employed for the precise assessment of Mineral Bone Disease (MBD). The search for reliable and non-invasive biochemical bone parameters has been ongoing for years [8].

The KDIGO suggests using total alkaline phosphatase activity as an adjunct test. This may provide further information in the assessment of MBD, particularly in case of increased PTH levels and for the assessment of response to therapy for increased PTH levels if liver disease is not suspected to be the cause of increased total alkaline phosphatase levels [2]. In adults, liver and bones express cell-membrane-associated enzyme called Alkaline phosphatase (ALP). Bone-specific alkaline phosphatase derives more specifically from osteoblasts cells & it affects bone mineralization [8]. Laboratory Analysis for t-ALP is inexpensive and therefore may be helpful for following patients response to therapy or determining MBD status when the comprehension of PTH is unclear [9]. Serum iPTH levels alone are insufficient to clearly distinguish adynamic or normal bone from hyper parathyroid bone disease. Therefore, the specificity of PTH as an indicator of MBD has been questioned [10].

Alkaline phosphatase may increase the predictive power of biochemical monitoring when taken into consideration concomitantly with PTH [11]. So, estimation of t-ALP has been used in this study as main biochemical indicator along with Parathormone as compared to previous studies which only stressed upon mineral (calcium and phosphorous) derangements in CKD patients.

### Methods/Approach:

A Cross-sectional observational study was conducted under the Department of Physiology on 330 CKD patients selected from dialysis unit, GSMCH, Patiala, over a period of four years. Patients with history of previous bone and skeletal disease (e.g. osteoporosis, achondroplasia, kyphoscoliosis etc.) unrelated to present ailment were excluded based on medical history (present and past) obtained from the patients. Approach to a Patient began by taking informed consent, after proper Medical examination. The detailed Medical history as well as baseline demographic data along with routine biochemical tests were recorded. Biochemical parameters like Serum alkaline phosphatase and Serum intact parathormone (iPTH), levels were analyzed by PNP-AMP (p-Nitro-phenyle phosphate-Amino Methyle Propanol) Kinetic method and FEIA (Fluorometric Enzyme Immuno-assay) method, respectively. Fully automated equipments standardized in Biochemistry laboratory were used for estimation of all parameters. Normal reference values (standardized as according to laboratory) of biochemical parameters were defined by KDIGO (2009) as mentioned below: -

- Serum iPTH=8.7 to 79.6pg/ml in Healthy subjects. In Dialysis Patients, serum iPTH=100 to 300 pg/ml; the cut off value was taken as 300pg/ml (2-9) times the upper limit of the normal laboratory assay.
- Serum alkaline phosphatase: 60-170IU/L

### Statistical Analysis-

SPSS (Statistical Package for Social Science) package was used to analyze descriptive statistics such as range, mean and standard deviation. To see association among different patterns of MBD (altered PTH levels) and other variables like demographic, clinical and biochemical characteristics of the study patients, Chi-square and ANOVA tests were used, and Correlation analysis was done among laboratory findings. The result was statistically significant when the P-value was less than 0.05. With the help of ANOVA test, results were expressed as mean±SD. For the measured analytes (biochemical parameters and age), One -way analysis of variance, and post-hoc analysis using tukey test were used to check for significance of difference. Individual plots were drawn to show the Mean changes in levels of iPTH and t-ALP for the above mentioned three main groups of MBD.

## RESULTS

Our results have shown that the high PTH levels were found to be more in CKD patients undergoing dialysis. All patients of CKD undergoing dialysis were categorized into three groups based on serum iPTH levels: Group A= Low iPTH level (serum iPTH<100 pg/ml) - "relative hypoparathyroidism" , Group B= Normal iPTH level (iPTH 100-300 pg/ml), Group C = High iPTH level (iPTH>300pg/ml)- "corresponding to hyperparathyroidism"

***Table 1. Association of MBD (altered PTH Levels) With Serum t-ALP level of the Study Patients***

| Laboratory Investigations | | iPTH Level | | | $\chi 2$ value | p-value |
|---|---|---|---|---|---|---|
| | | Low (<100) | Normal (100 – 300) | High (>300) | | |
| tALP Level | Below Normal | 0 (0.0%) | 1 (50.0%) | 1 (50.0%) | 10.331 | 0.035* |
| | Normal | 47 (36.2%) | 42 (32.3%) | 41 (31.5%) | | |
| | Above Normal | 41 (31.3%) | 26 (19.8%) | 64 (48.9%) | | |

The statistical analysis with $\chi 2$ testing of the results revealed that MBD is significantly associated with t-ALP level (p value was < 0.05, significant).

***Table 2. Mean t-ALP and MBD (altered PTH level)***

| GROUPS | N | tALP Mean ± SD | ANOVA# | Comparison | p-value# |
|---|---|---|---|---|---|
| A. Low iPTH Level | 88 | 200.83 ± 130.06 | F = 8.032; p < 0.001; Highly significant | A vs B | $0.987^{NS}$ |
| B. Normal iPTH Level | 69 | 191.79 ± 141.38 | | A vs C | 0.002* |
| C. High iPTH Level | 106 | 377.70 ± 540.86 | | B vs C | 0.003* |

Higher t-ALP values with its upper range (60-170 IU/L) was obtained in hyper parathyroid patients than in hypo parathyroid patients. The difference was statistically highly significant(p<0.001).

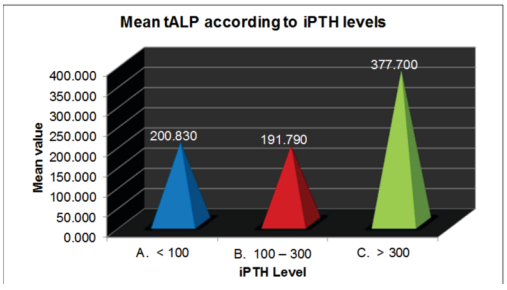


***Figure 1. Mean t-ALP according to iPTH levels***

## DISCUSSION

It was observed that alterations in biochemical profile were common in CKD patients. In our study, t-ALP level >170 IU/L (i.e., upper level of normal) was present in 49.4% of CKD patients. Higher t-ALP values with its upper range was obtained with the participants falling in high PTH range (Mean Value =377.70) than low PTH range (Mean Value=200.83).Cutoff for t-ALP was >170IU/L. Statistically differences in t-ALP between all groups were found to be highly significant (p<0.001).

iPTH level is directly linked with t-ALP with significant p value (p=0.035,) as was proved with the ANOVA test of three inter group comparisons of iPTH level, that High and normal PTH levels were more significantly associated with t-ALP level (p= 0.002 and p= 0.003, respectively) as compared to low PTH levels (p=0.987). Estimation of iPTH and t-ALP for diagnosis of MBD in dialysis patients shows an increasing trend as is also accepted by KDIGO 2009. Jabbar et al. (2007) found raised bone alkaline phosphatase (b-ALP) in 60% of their stage 5 of CKD patients [12]. Similarly, Budhathoki et al (2015) found that serum alkaline phosphatase (t-ALP), was significantly high in CKD patients, which is also a biochemical marker of MBD and is used to monitor the metabolic bone disease associated with renal insufficiency [13]. But, Okeyo et al (2015) stated that total alkaline phosphatase was not found to be a good surrogate marker for CKD-MBD in his study. It did not correlate with early markers - serum PTH and vitamin D [5].

Short of a bone biopsy, biochemical tests such as total alkaline phosphatase or intact PTH can be used to evaluate bone disease because markedly high or low values do predict underlying bone disease.

## CONCLUSION

This study rejects the null hypothesis and accepts the alternate hypothesis that there is a statistically significant association of t-ALP levels with MBD (altered iPTH levels) for CKD patients on haemodialysis.

### Future Scope of this Study

Despite notable advances in the technology to provide dialysis, the mortality rate of patients on long-term dialysis has remained disappointingly high and not significantly enhanced over many decades. As MBD in CKD remains a major challenge; hence, improving means of early detection is the key to deal with this issue, and this study may possibly help in developing strategies in bettering clinical outcome of CKD patients.

### Compliance with Ethical Standards

**Conflict of interest:** This research did not receive any specific grant from any funding agency in the public, commercial, or non-profits organizations.

**Ethical standards:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and all patients gave the informed consent prior being included into the study. This study was approved by the Research Ethics Committee (or Institutional Review Board)".

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