MEDS Public Health and Preventive Medicine (2025)
Clausius Scientific Press, Canada

DOI: 10.23977/phpm.2025.050119
ISSN 2616-1915 Vol. 5 Num. 1

# *Changes in Serum PINP and β-CTX Levels before and after Glucocorticoid Therapy in Patients with Systemic Lupus Erythematosus and Their Clinical Significance*

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***Keywords:*** Systemic Lupus Erythematosus; Glucocorticoids; PINP; β-CTX

***Abstract:*** This study aims to elucidate the characteristics of bone metabolic imbalance and its clinical significance as reflected by the changes in serum PINP and β-CTX levels before and after glucocorticoid therapy in patients with systemic lupus erythematosus (SLE). The results indicate a rapid decline in PINP levels during the early phase of treatment, suggesting a marked suppression of bone formation, while β-CTX levels, though showing delayed elevation in some cases, remained indicative of active bone resorption overall, demonstrating that a bidirectional imbalance in bone metabolism had already developed as a systemic stress response in the short term. Analysis of these biomarkers contributes to the establishment of individualized bone health monitoring models for SLE patients, providing an evidence-based foundation for risk management during glucocorticoid therapy.

## 1. Introduction

Systemic lupus erythematosus (SLE), characterized by immune dysregulation and multi-organ involvement, relies heavily on glucocorticoids for their anti-inflammatory and immunosuppressive effects; however, the impact of such treatment on bone metabolism warrants close attention, particularly due to the suppression of bone formation and disruption of bone resorption associated with long-term use. Clinical observations indicate that SLE patients face a significantly higher risk of fractures compared to the general population, with early-stage bone alterations often lacking overt clinical manifestations and eluding timely detection by imaging alone. The selection of highly sensitive and specific biochemical markers to identify early signs of bone metabolic imbalance has become essential for guiding therapeutic strategies and evaluating skeletal health. This study centers on two key bone turnover markers, PINP and β-CTX, examining their dynamic changes before and after glucocorticoid treatment and the physiological mechanisms these changes reveal.

## 2. The Impact Pathways of Glucocorticoids on Bone Metabolism in SLE Patients

### 2.1 Imbalance between Bone Formation and Resorption Induced by Glucocorticoids

As a cornerstone in the treatment of systemic lupus erythematosus (SLE), long-term

administration of glucocorticoids has been demonstrated to profoundly disrupt bone metabolism. While effectively suppressing proinflammatory cytokine activity, glucocorticoids significantly impair the differentiation and function of osteoblasts, resulting in diminished bone formation. In contrast, the inhibitory effect on osteoclast activity remains relatively limited, leading to an unsynchronized suppression of bone resorption. This disequilibrium drives a systemic shift in bone metabolic homeostasis, culminating in reduced bone mineral density and a markedly increased risk of osteoporosis. In this pathological context, changes in serum levels of procollagen type I N-terminal propeptide (PINP) and β-C-terminal telopeptide of type I collagen (β-CTX), serving as biomarkers for bone formation and resorption respectively, offer valuable insight into the hormonally mediated remodeling status of bone tissue.

Of particular note, glucocorticoids modulate osteoclast activity by interfering with the RANK/RANKL/OPG signaling axis. Simultaneously, adrenocortical steroids alter the Wnt/β-catenin pathway and its downstream regulators, which play a pivotal role in suppressing osteogenesis. This disruption in the micro-level coordination between bone formation and resorption gives rise to a characteristic metabolic profile marked by decreased PINP and relatively elevated β-CTX. Such a biochemical signature highlights the necessity of incorporating bone metabolism monitoring into the therapeutic framework for SLE, thereby strengthening the evaluation of risk associated with hormonal intervention.

### 2.2 Revealing the Dynamic Relationship between PINP and β-CTX Pre- and Post-Treatment

A systematic analysis of the temporal variations in PINP and β-CTX levels before and after glucocorticoid treatment in SLE patients reveals that their dynamic evolution does not follow a linear trajectory. A rapid divergence between the two biomarkers becomes evident during the early phase of therapy, with PINP levels declining sharply ahead of any notable fluctuation in β-CTX, resulting in a clinical pattern characterized by acutely suppressed bone formation and relatively lagging resorption. This imbalance tends to stabilize during maintenance therapy, indicating a persistent burden on bone metabolism [1].

Longitudinal comparisons of biomarker fluctuations before and after treatment show that PINP levels undergo a marked reduction within the initial weeks of glucocorticoid administration, while β-CTX, although partially affected, remains at a comparatively elevated level. The sustained high-turnover state reflects continuous interference with the bone remodeling system beyond anti-inflammatory modulation. These findings underscore the importance of incorporating bone-protective strategies into therapeutic planning and advocate for the inclusion of dynamic bone metabolic markers to achieve personalized risk management in clinical practice.

### 2.3 Systemic Repositioning of Bone Tissue Function under Hormonal Influence

The influence of glucocorticoids on bone tissue extends beyond biochemical parameters and surpasses the localized physiological boundaries of the osteon. It disrupts the homeostatic regulation of the bone marrow microenvironment, angiogenesis, and immune cell migration, initiating a systemic adaptive response centered on the repositioning of bone metabolic functions. The concurrent decline in PINP and fluctuation in β-CTX occur alongside a comprehensive reprogramming of cytokine profiles within the bone microenvironment, reflecting a profound transformation from structural integrity to functional adaptation.

Chronic hormonal intervention shifts bone function from mechanical support toward an endocrine-mediated regulatory role. This adaptive shift, rather than mitigating bone tissue loss, may obscure the cumulative structural risks associated with abnormal bone turnover, resulting in delayed recognition of subclinical osteoporosis and fracture susceptibility. Therefore, evaluating variations

in PINP and β-CTX should be integrated with imaging modalities and microstructural assessments, forming a multi-dimensional interpretive model that spans molecular, tissue, and functional levels [2].

## 3. Temporal Dynamics and Clinical Interpretation of Serum PINP and β-CTX Fluctuations

### 3.1 Early-Stage Biomarker Volatility and Its Correlation with Inflammatory Control

During the initial phase of glucocorticoid intervention in systemic lupus erythematosus (SLE), significant disturbances emerge within the internal homeostasis of bone metabolism, reflected by non-linear short-term fluctuations in serum levels of PINP and β-CTX. These changes are not solely attributable to direct alterations in bone turnover, but rather stem from the interplay between the rate of pro-inflammatory cytokine reduction and the bone tissue's sensitivity to steroid signaling. As inflammatory mediators rapidly decline, PINP levels typically exhibit suppression due to inhibited osteoblastic activity, whereas β-CTX may show transient elevation associated with brief increases in osteoclastic activity, forming a dynamic window where metabolic shifts align closely with immune modulation.

During this period, biomarker fluctuations closely mirror the extent of inflammatory suppression, though the magnitude and temporal rhythm vary across individuals. These responses fundamentally reflect bone metabolism’s stress adaptation to immunological restructuring driven by glucocorticoids. As such, PINP and β-CTX function as biochemical nodes at the interface between inflammation resolution and skeletal homeostasis disruption, and their interpretation requires an integrated understanding of SLE’s multisystemic interactions.

### 3.2 Intermediate and Stable Phase Trends as Indicators of Treatment Rhythm

As treatment advances into the intermediate and relatively stable phases, glucocorticoid dosages stabilize and the body enters a phase of hormonal adaptation. At this point, the influence of inflammatory activity on PINP and β-CTX levels diminishes, giving rise to more regular and steady metabolic patterns. Although the tension between suppressed bone formation and elevated resorption becomes more balanced, this does not indicate true recovery but rather a recalibrated metabolic set-point. The delayed rebound in PINP alongside sustained elevation of β-CTX highlights an asymmetrical adaptation in bone remodeling mechanisms.

Such biomarker trends illuminate the adaptive processes of skeletal tissues under prolonged glucocorticoid exposure and provide a biological foundation for modulating treatment tempo [3]. The stabilized trajectories of bone metabolism markers in serum reflect the latent integration of pharmacological effects within skeletal systems. These temporal patterns not only indicate the sustained metabolic reverberations of therapy but also serve as intrinsic indicators of the transition into remission and maintenance phases, demonstrating substantial value in clinical monitoring.

### 3.3 Coupling Mechanisms between Bone Metabolism and SLE Disease Activity

Bone metabolic markers function within a broader biochemical context, maintaining deep systemic correlations with the immunological activity of SLE. Particularly in chronic inflammatory states, dysregulation of bone formation and resorption has shown significant association with disease activity indices. The concurrent decline in PINP and elevation in β-CTX is not merely a result of local skeletal stress, but rather a systemic metabolic feedback loop orchestrated by persistent immune activation, highlighting a co-constructed pathological pathway between the immune and skeletal systems.

Longitudinal observations reveal that changes in serum markers often precede fluctuations in clinical symptoms, suggesting their potential role in predicting cycles of disease activity. In subclinical states, the heightened sensitivity of bone metabolism may act as a compensatory signal, indicating a shift in the regulation of the immune-bone axis. The non-equilibrium stability expressed by dynamic fluctuations of PINP and β-CTX serves not only as an indicator of therapeutic response but also as a critical lens through which to examine the pathophysiological rhythm of SLE.

## 4. The Logical Basis and Limitations of PINP and β-CTX as Monitoring Tools

### 4.1 Applicability of Biomarkers in Complex Pathophysiological Contexts

Systemic lupus erythematosus (SLE), as a multisystem autoimmune disorder, is characterized by immune dysregulation and systemic inflammation, both of which contribute to widespread metabolic imbalances. Glucocorticoid therapy, while effective in modulating disease activity, concurrently disrupts intrinsic bone metabolic pathways. Under such systemic conditions, serum levels of PINP and β-CTX—representing bone formation and resorption respectively—must be interpreted within the broader context of inflammatory responses and immune-mediated mechanisms to avoid reductive or decontextualized conclusions.

Given the high heterogeneity in SLE pathogenesis, metabolic responses to glucocorticoid therapy also vary significantly among individuals, making it difficult to rely on bone biomarkers as stand-alone evaluative tools. Instead, comprehensive assessment integrating disease activity, steroid exposure intensity, and other metabolic variables is necessary to elucidate the true physiological implications of observed changes in serum biomarkers, particularly in cases involving disease fluctuation or multi-organ involvement, where interpretive accuracy must be calibrated across multiple clinical dimensions [4].

### 4.2 Complementarity between Biochemical and Traditional Assessment Methods

Unlike traditional bone mineral density (BMD) testing that primarily evaluates structural bone mass, PINP and β-CTX reflect the rate and direction of bone turnover at the molecular level, offering a temporal advantage in capturing early metabolic shifts. Because BMD assessments are less sensitive to short-term bone changes induced by glucocorticoids, the integration of serum markers enhances real-time monitoring of bone metabolic dynamics, especially during the initial phase of treatment, providing biological feedback regarding the alignment between steroid dosage and skeletal response.

However, from a clinical interpretative standpoint, BMD and biochemical markers represent fundamentally different layers of bone health and cannot be viewed as interchangeable. They should function as complementary components in the diagnostic framework. Combining structural imaging data with dynamic metabolic indices allows for a more holistic understanding of bone status across both temporal and pathological spectra, thereby improving the detection of subtle but progressive changes during long-term therapy.

### 4.3 Impact of Individual Variability on Biomarker Interpretation Accuracy

Individual variability in metabolic baselines, hormonal levels, and comorbid conditions among SLE patients introduces significant heterogeneity in therapeutic responses and biomarker expressions, leading to asynchronous bone metabolic reactions despite identical glucocorticoid dosing. In some patients, marked fluctuations in serum PINP and β-CTX are not accompanied by

detectable changes in BMD or clinical symptoms, while others may experience pronounced bone loss despite relatively stable biomarker levels, underscoring the disruptive influence of individual metabolic traits.

Variables such as sex, age, menopausal status, nutritional intake, renal function, and steroid metabolism enzyme activity can introduce non-pathological interferences to PINP and β-CTX readings, thereby diminishing their generalizability and interpretive consistency [5]. Clinical application of these biomarkers should not be decoupled from patient-specific contextual factors. Instead, their interpretation must be supported by a multidimensional analysis that integrates clinical parameters, laboratory data, and medical history to avoid misjudgments stemming from rigid adherence to reference values.

## 5. Conclusion

Glucocorticoids, while modulating immune responses in SLE, significantly disrupt the intrinsic balance of bone metabolism, as evidenced by a marked decrease in PINP and a relative increase in β-CTX, jointly indicating an asymmetric response characterized by suppressed bone formation and insufficiently controlled bone resorption. This biochemical profile reflects the systemic impact of glucocorticoid therapy on the skeletal system and provides a quantitative basis for assessing bone metabolic risk and formulating intervention strategies. Dynamic monitoring of these biomarkers during treatment should be considered an integral component of SLE management.

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