RESEARCH PAPER

Comparative Evaluation of Alkaline Phosphatase and Cathepsin-B Levels in Gingival Crevicular Fluid During Orthodontic Tooth Movement with Conventional Brackets, Self-Ligating Brackets, and Clear Aligners

Dr. Rahul Paul[1*], Dr. Deepti Yadav[2], Dr. Ish Kumar Sharma[3], Dr. Ratika Shawney[4], Dr. Rohit Tiwari[5]

[1]Principal & Head of the Department, Department of Orthodontics & Dentofacial Orthopaedics, Inderprastha Dental College & Hospital, Email: drrahulpaul@Gmail.com.*

[2]Professor, Department of Orthodontics & Dentofacial Orthopaedics, Inderprastha Dental College & Hospital.

[3]Reader, Department of Orthodontics & Dentofacial Orthopaedics, Inderprastha Dental College & Hospital

[4]Senior Lecturer, Department of Orthodontics & Dentofacial Orthopedics, Inderprastha Dental College & Hospital.

[5]Post Graduate Student, Department of Orthodontics & Dentofacial Orthopaedics, Inderprastha Dental College & Hospital.

ABSTRACT

Introduction: Orthodontic tooth movement is a biologically regulated process involving periodontal ligament remodeling and alveolar bone turnover. Biochemical markers present in gingival crevicular fluid (GCF), such as alkaline phosphatase (ALP) and cathepsin-B (CTSB), provide valuable insight into osteoblastic and osteoclastic activity during orthodontic treatment. However, comparative data on these biomarkers across different orthodontic appliance systems remain limited.

Materials and Methods: This prospective, randomized clinical study included 30 post-pubertal patients undergoing non-extraction orthodontic treatment. Subjects were randomly allocated into three groups (n = 10 each): Group A (conventional MBT brackets), Group B (self-ligating brackets), and Group C (clear aligners). GCF samples were collected from the mesial aspect of the right maxillary canine at four standardized time intervals (T0–T3). ALP and CTSB levels were quantified using enzyme-linked immunosorbent assay (ELISA). Intragroup comparisons were performed using paired t-tests, and intergroup comparisons were analyzed using one-way ANOVA, with significance set at $p \leq 0.05$.

Results: All three groups demonstrated statistically significant temporal changes in ALP and CTSB levels. In Group A, ALP increased progressively from 14.20 ± 3.02 ng/mL at T0 to 45.89 ± 9.87 ng/mL at T3 ($p < 0.001$), while CTSB peaked at T2 (711.7 ± 18.57 pg/mL) before declining. Group B showed similar trends with lower magnitude (ALP: 14.93 ± 2.12 to 42.14 ± 3.83 ng/mL; CTSB peak: 634.8 ± 16.46 pg/mL). Group C demonstrated moderated responses with ALP rising from 14.4 ± 1.79 to 29.83 ± 7.91 ng/mL at T1, followed by stabilization. Intergroup comparison revealed significant differences among all groups at all time intervals ($p < 0.001$), with conventional brackets showing the highest biomarker levels, followed by self-ligating brackets, and aligners exhibiting the lowest responses.

Conclusion: Orthodontic appliance systems significantly influence the biological response of periodontal tissues. Conventional fixed appliances elicit the greatest bone remodeling activity, followed by self-ligating brackets, while clear aligner therapy produces a more controlled biochemical response. These findings provide a biologic rationale for appliance selection based on both mechanical efficiency and tissue compatibility.

Keywords: Orthodontic tooth movement, Gingival crevicular fluid, Alkaline phosphatase, Cathepsin-B, Conventional brackets, Self-ligating brackets, Clear aligners.

How To Cite This Article: Paul R, Yadav D, Sharma Ik, Shawney R, Tiwari R. Comparative Evaluation Of Alkaline Phosphatase And Cathepsin-B Levels In Gingival Crevicular Fluid During Orthodontic Tooth Movement With Conventional Brackets, Self-Ligating Brackets, And Clear Aligners. Int J Drug Deliv Technol. 2026;16(26s):99-106. Doi: 10.25258/ijddt.16.26s.10

1. INTRODUCTION

Orthodontic tooth movement (OTM) is a biologically regulated process initiated by the application of controlled mechanical forces, leading to coordinated cellular and molecular responses within the periodontal ligament and surrounding alveolar bone[1]. Rather than being a purely mechanical displacement of teeth, OTM involves a dynamic interaction between periodontal tissues that allows controlled tooth movement while preserving periodontal integrity[2].

Early histological investigations established the biological basis of orthodontic tooth movement. Classic studies demonstrated that orthodontic force application creates distinct pressure and tension zones within the periodontal ligament, resulting in localized bone resorption on the pressure side and bone formation on the tension side[3,4].

These findings confirmed that tooth movement occurs through a process of alveolar bone remodeling rather than direct mechanical shifting of teeth.

The periodontal ligament plays a central role in mediating orthodontic force response due to its mechanosensitive nature. It converts mechanical loading into biochemical signals that regulate cellular activity and alveolar bone remodeling, thereby governing the rate and quality of tooth movement[5]. Alterations in vascularity, cellular morphology, and tissue metabolism within the periodontal ligament initiate a cascade of biological events essential for orthodontic tooth displacement.

The magnitude and duration of orthodontic force significantly influence periodontal tissue responses. Excessive forces may result in periodontal ligament hyalinization and delayed tooth movement, whereas light and continuous forces promote efficient frontal bone resorption with minimal tissue damage[6]. Contemporary research has further established orthodontic tooth movement as a controlled inflammatory process involving the release of cytokines, prostaglandins, and growth factors that regulate osteoclastic and osteoblastic activity during bone remodeling[7].

Gingival crevicular fluid (GCF) has emerged as a reliable, non-invasive medium for monitoring periodontal tissue metabolism during orthodontic treatment[14]. It contains various enzymes, inflammatory mediators, and bone remodeling markers that reflect the biological events occurring within the periodontium. Among these biomarkers, alkaline phosphatase (ALP) serves as an indicator of osteoblastic activity and bone formation, while cathepsin-B (CTSB) reflects osteoclastic activity and extracellular matrix degradation during bone resorption.

The present study was undertaken to evaluate and compare the changes in ALP and CTSB levels in GCF during orthodontic tooth movement using three different orthodontic modalities: conventional preadjusted edgewise appliances, self-ligating brackets, and clear aligners. The null hypothesis stated that there would be no statistically significant difference in biomarker levels among the three treatment groups.

2. MATERIALS AND METHODS

2.1 Study Design and Sample Selection

This prospective longitudinal study was conducted in the Department of Orthodontics and Dentofacial Orthopaedics, Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad, India. A total of 30 patients requiring orthodontic treatment were selected and randomly divided into three groups of 10 patients each:

- **Group A:** Conventional preadjusted edgewise appliances (Mini Diamond Ormco, 0.022" slot MBT prescription)
- **Group B:** Self-ligating brackets (Damon system)
- **Group C:** Clear aligner therapy (ODS aligners)

Figure 01: GCF Collection from the mesial aspect of the right maxillary canine

2.2 GCF Collection Protocol

Gingival crevicular fluid samples were collected from the mesial aspect of the right maxillary canine(Figure 01) under standardized clinical conditions at four time intervals:

For Group A (Conventional Brackets):

- T0: Before commencement of orthodontic treatment
- T1: After one month with 0.016" NiTi archwire
- T2: After one month with 0.017×0.025" NiTi archwire
- T3: After one month with 0.017×0.025" Stainless steel archwire

For Group B (Self-Ligating Brackets):

- T0: Before commencement of orthodontic

treatment
- T1: After one month with 0.014" CuNiTi archwire
- T2: After one month with 0.014×0.025" CuNiTi archwire
- T3: After one month with 0.018×0.025" CuNiTi archwire

For Group C (Clear Aligners):
- T0: Before commencement of orthodontic treatment
- T1: After completion of 2 sets of aligners
- T2: After completion of 4 sets of aligners
- T3: After completion of 6 sets of aligners

2.3 Collection Procedure
The selected site was isolated with cotton rolls, air-dried, and supragingival plaque was gently removed without entering the sulcus. GCF was collected atraumatically using microcapillary tubes placed at the orifice of the gingival sulcus without penetrating the sulcus. Samples contaminated with blood were discarded. Collected samples were immediately transferred to labeled Eppendorf tubes and stored at −20°C until biochemical analysis.

2.4 Biochemical Analysis
ALP and CTSB levels were quantified using commercially available ELISA kits (ERBA Mannheim LISASCAN EM) according to the manufacturer's protocols. All samples were analyzed in duplicate to ensure accuracy.

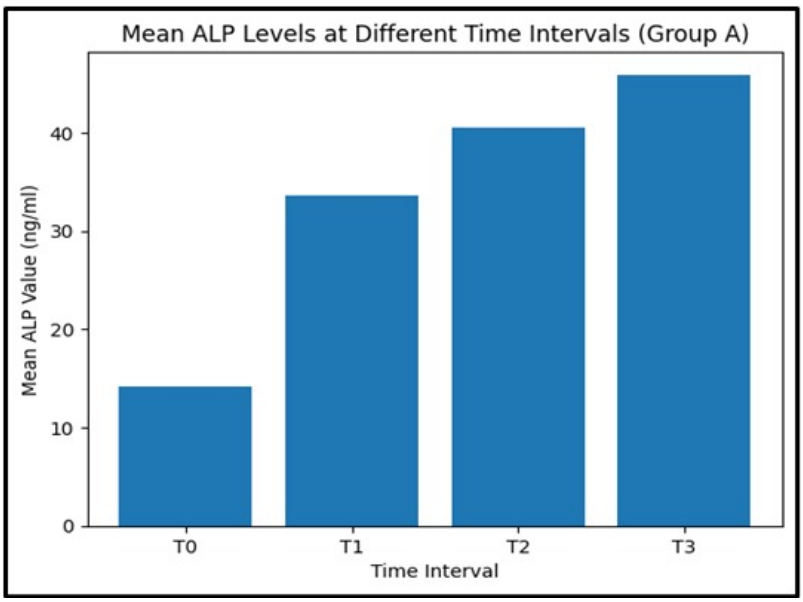
2.5 Statistical Analysis
Data were recorded in Microsoft Excel 2010 and analyzed using SPSS software (version 27.0). Descriptive statistics were expressed as mean and standard deviation. Intragroup comparisons were performed using paired t-test, while intergroup comparisons were analyzed using one-way ANOVA followed by post-hoc tests. The level of significance was set at $p<0.05$.

3. RESULTS
All 30 patients completed the study without adverse events or complications. The mean age of participants was comparable across groups, and no significant differences in baseline clinical parameters were observed.

3.1 Changes in Alkaline Phosphatase Levels
Group A (Conventional Brackets): ALP levels showed a progressive and statistically significant increase throughout treatment (Table 1, Figure 1). Mean ALP values increased from 14.20 ± 3.02 ng/mL at T0 to 33.58 ± 11.15 ng/mL at T1, 40.53 ± 9.85 ng/mL at T2, and 45.89 ± 9.87 ng/mL at T3. Paired comparisons revealed significant increases at all intervals: T1-T0 (mean difference = 19.38 ng/mL; p = 0.001), T2-T1 (mean difference = 6.95 ng/mL; p < 0.001), T3-T2 (mean difference = 5.36 ng/mL; p < 0.001), and T3-T0 (mean difference = 31.69 ng/mL; p < 0.001).

Table 1: Alkaline Phosphatase Levels (ng/mL) in Group A (Conventional Brackets)

Time Interval	Mean ± SD	Paired Comparison	Mean Difference	t-value	p-value
T0	14.20± 3.02	T1-T0	19.38 ± 12.41	-4.940	0.001,S
T1	33.58± 11.15	T2-T1	6.95 ± 3.21	-6.847	<0.001,HS
T2	40.53 ± 9.85	T3-T2	5.36 ± 0.36	-46.732	<0.001,HS
T3	45.89 ± 9.87	T3-T0	31.69 ± 11.25	-8.910	<0.001,HS

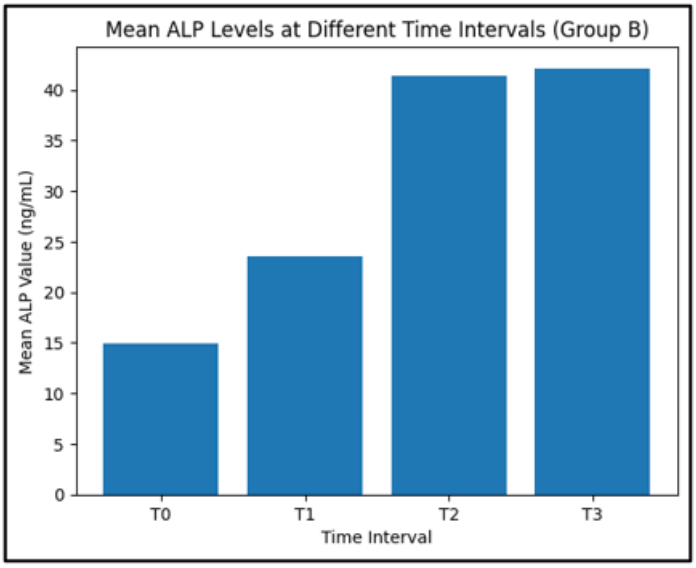


Group B (Self-Ligating Brackets): ALP levels demonstrated a progressive increase (Table 2, Figure 2). Mean values rose from 14.93 ± 2.12 ng/mL at T0 to 23.58 ± 1.34 ng/mL at T1, 41.33 ± 3.77 ng/mL at T2, and 42.14 ± 3.83 ng/mL at T3.

All paired comparisons showed highly significant increases ($p < 0.001$), with T3-T0 mean difference of 27.21 ± 4.32 ng/mL.

Table 2: Alkaline Phosphatase Levels (ng/mL) in Group B (Self-Ligating Brackets)

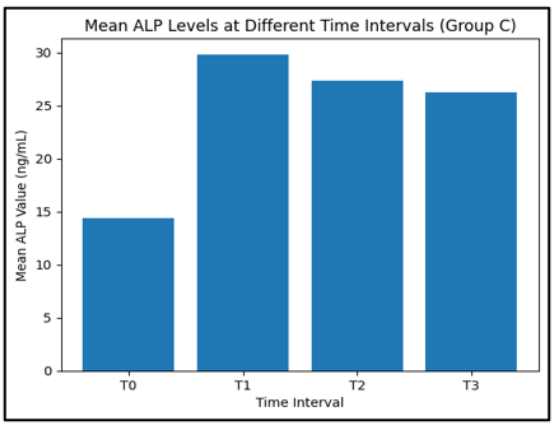
Time Interval	Mean± SD	Paired Comparison	Mean Difference	t-value	p-value
T0	14.93± 2.12	T1-T0	17.42 ± 3.84	-14.342	<0.001,HS
T1	23.58± 1.34	T2-T1	8.98 ± 0.79	-36.013	<0.001,HS
T2	41.33 ± 3.77	T3-T2	0.81 ± 0.26	-9.689	<0.001,HS
T3	42.14 ± 3.83	T3-T0	27.21 ± 4.32	-19.897	<0.001,HS



Group C (Clear Aligners): ALP levels showed an initial increase followed by stabilization (Table 3, Figure 3). Mean values increased from 14.40 ± 1.79 ng/mL at T0 to 29.83 ± 7.91 ng/mL at T1 ($p = 0.001$), then slightly declined to 27.39 ± 1.42 ng/mL at T2 and 26.21 ± 1.43 ng/mL at T3. The T3-T2 comparison showed a significant decrease (mean difference = -1.18 ng/mL; $p < 0.001$), while T3-T0 showed a significant net increase (mean difference = 11.81 ± 1.90 ng/mL; $p < 0.001$).

Table 3: Alkaline Phosphatase Levels (ng/mL) in Group C (Clear Aligners)

Time Interval	Mean ± SD	Paired Comparison	Mean Difference	t-value	p-value
T0	14.40 ± 1.79	T1-T0	9.18 ± 1.73	-16.824	0.001,S
T1	29.83 ± 7.91	T2-T1	3.81 ± 0.28	-42.926	<0.001,HS
T2	27.39 ± 1.42	T3-T2	-1.18 ± 0.04	88.500	<0.001,HS
T3	26.21 ± 1.43	T3-T0	11.81 ± 1.90	-19.614	<0.001,HS



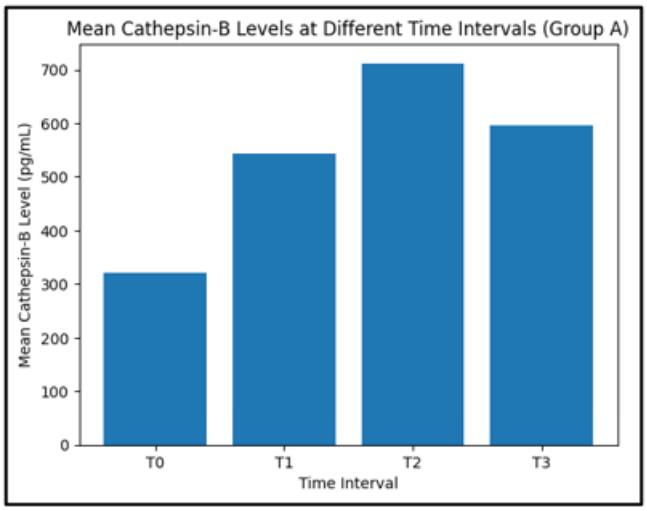
3.2Changes in Cathepsin-B Levels

Group A (Conventional Brackets): CTSB levels demonstrated a characteristic peak-and-decline pattern (Table 4, Figure 4). Mean values increased from 321.0 ±

10.83 pg/mL at T0 to 542.9 ± 19.42 pg/mL at T1, peaked at 711.7 ± 18.57 pg/mL at T2, and declined to 596.2 ± 18.44 pg/mL at T3. All paired comparisons were highly significant ($p < 0.001$), with T3-T0 net increase of 275.20 ± 8.55 pg/mL.

Table 4: Cathepsin-B Levels (pg/mL) in Group A (Conventional Brackets)

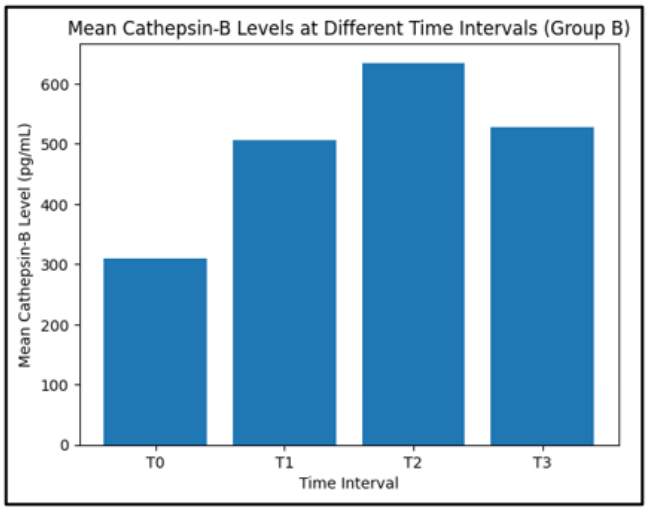
Time Interval	Mean ± SD	Paired Comparison	Mean Difference	t-value	p-value
T0	321.0 ± 10.83	T1-T0	221.9 ± 8.90	-78.843	<0.001,HS
T1	542.9 ± 19.42	T2-T1	168.8 ± 4.92	-108.559	<0.001,HS
T2	711.7 ± 18.57	T3-T2	-115.5 ± 2.12	172.177	<0.001,HS
T3	596.2 ± 18.44	T3-T0	275.20 ± 8.55	-101.810	<0.001,HS



Group B (Self-Ligating Brackets): CTSB levels showed a similar pattern with lower magnitude (Table 5, Figure 5). Mean values increased from 309.8 ± 9.00 pg/mL at T0 to 505.5 ± 16.70 pg/mL at T1, peaked at 634.8 ± 16.46 pg/mL at T2, and declined to 527.1 ± 16.59 pg/mL at T3. All paired comparisons were highly significant ($p < 0.001$).

Table 5: Cathepsin-B Levels (pg/mL) in Group B (Self-Ligating Brackets)

Time Interval	Mean ± SD	Paired Comparison	Mean Difference	t-value	p-value
T0	309.8 ± 9.00	T1-T0	195.7 ± 7.99	-77.485	<0.001,HS
T1	505.5 ± 16.70	T2-T1	129.3 ± 4.42	-92.436	<0.001,HS
T2	634.8 ± 16.46	T3-T2	-107.7 ± 1.06	321.497	<0.001,HS
T3	527.1 ± 16.59	T3-T0	217.3 ± 7.76	-88.540	<0.001,HS

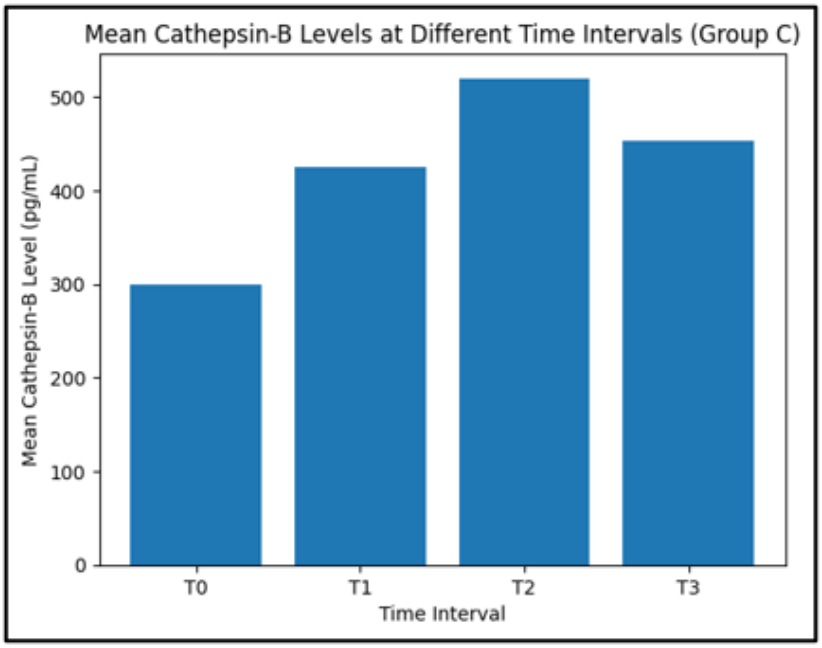


Group C (Clear Aligners): CTSB levels demonstrated moderated responses (Table 6, Figure 6). Mean values increased from 299.8 ± 9.00 pg/mL at T0 to 424.8 ± 15.05 pg/mL at T1, 520.3 ± 15.97 pg/mL at T2, and declined to

454.0 ± 13.89 pg/mL at T3. All paired comparisons were highly significant ($p < 0.001$).

Table 6: Cathepsin-B Levels (pg/mL) in Group C (Clear Aligners)

Time Interval	Mean ± SD	Paired Comparison	Mean Difference	t-value	p-value
T0	299.8 ± 9.00	T1-T0	125.0 ± 6.09	-64.887	<0.001,HS
T1	424.8 ± 15.05	T2-T1	95.5 ± 2.07	-146.014	<0.001,HS
T2	520.3 ± 15.97	T3-T2	-66.3 ± 2.31	90.691	<0.001,HS
T3	454.0 ± 13.89	T3-T0	154.2 ± 5.16	-94.507	<0.001,HS



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3.3 Intergroup Comparisons

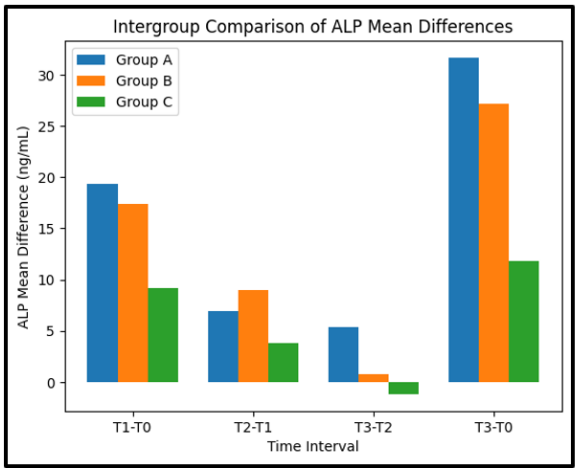
Intergroup analysis revealed significant differences among the three groups for both biomarkers at all time intervals (Table 7).

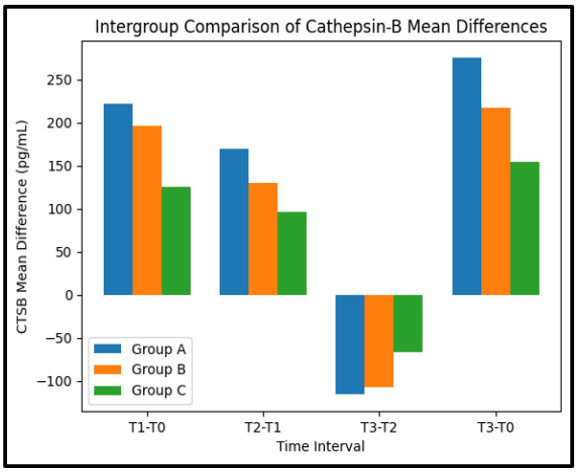
ALP Comparisons: At T1-T0, Group A showed the greatest increase (19.38 ± 12.41 ng/mL), followed by Group B (17.41 ± 3.84 ng/mL) and Group C (9.18 ± 1.73 ng/mL) ($p = 0.013$). At T2-T1 and T3-T2, highly significant differences were observed ($p < 0.001$). The overall T3-T0 comparison showed significantly higher ALP increase in Group A (31.68 ± 11.25 ng/mL) compared to Group B (27.21 ± 4.32 ng/mL) and Group C (11.81 ± 1.90 ng/mL) ($p < 0.001$).

CTSB Comparisons: Highly significant intergroup differences were observed at all intervals ($p < 0.001$). At T1-T0, Group A showed the greatest increase (221.90 ± 8.90 pg/mL), followed by Group B (195.70 ± 7.99 pg/mL) and Group C (125.00 ± 6.09 pg/mL). Similar trends were maintained throughout treatment, with T3-T0 net increases of 275.20 ± 8.55 pg/mL (Group A), 217.30 ± 7.76 pg/mL (Group B), and 154.20 ± 5.16 pg/mL (Group C).

Table 7: Intergroup Comparison of ALP and CTSB Mean Differences

Time Interval	Group A	Group B	Group C	F-value	p-value
ALP (ng/mL)					
T1-T0	19.38 ± 12.41	17.41 ± 3.84	9.18 ± 1.73	5.120	0.013,S
T2-T1	6.95 ± 3.21	8.98 ± 0.79	3.81 ± 0.28	18.499	<0.001,HS
T3-T2	5.35 ± 0.36	0.81 ± 0.26	-1.18 ± 0.04	1659.125	<0.001,HS
T3-T0	31.68 ± 11.25	27.21 ± 4.32	11.81 ± 1.90	21.919	<0.001,HS
CTSB (pg/mL)					
T1-T0	221.90 ± 8.90	195.70 ± 7.99	125.00 ± 6.09	418.479	<0.001,HS
T2-T1	168.80 ± 4.92	129.30 ± 4.42	95.50 ± 2.07	840.817	<0.001,HS
T3-T2	-115.50 ± 2.12	-107.70 ± 1.06	-66.30 ± 2.31	1912.815	<0.001,HS
T3-T0	275.20 ± 8.55	217.30 ± 7.76	154.20 ± 5.16	687.053	<0.001,HS





4. DISCUSSION

Orthodontic tooth movement is a biologically regulated process involving coordinated cellular and molecular responses within the periodontal ligament and alveolar bone[1–7]. The pressure-tension theory remains fundamental, explaining bone resorption on the compression side and formation on the tension side[2–4,8,9]. Gingival crevicular fluid (GCF) is a reliable, non-invasive medium for monitoring these biologic events[14,15].

In the present study, alkaline phosphatase (ALP) levels showed a progressive increase in all groups, reflecting sustained osteoblastic activity and bone formation, consistent with previous reports[8,11,16–18]. The conventional bracket group (Group A) demonstrated the greatest increase in ALP (76%), attributable to continuous force application and prolonged periodontal stimulation[3–6,8]. The self-ligating bracket group (Group B) exhibited a significant but lower rise (52%), explained by reduced friction and lighter force systems resulting in efficient yet controlled bone remodeling[13,19,22]. Clear aligner therapy (Group C) showed an initial rise followed by stabilization (32% increase), reflecting intermittent force delivery and partial periodontal recovery between activations, which may provide a more physiologically compatible stimulus[14,19].

Cathepsin-B (CTSB) levels increased during early and intermediate phases in all groups, indicating active osteoclastic and proteolytic activity associated with compression-side remodeling[10,20]. The subsequent reduction in CTSB at later stages (T3) suggests progression toward periodontal stabilization and reparative remodeling, consistent with a biphasic, phase-specific pattern of biomarker expression[10,21]. These findings align with the concept of tightly regulated proteolytic activity, where an initial rise in CTSB is later balanced by its inhibitors[12].

Intergroup comparison confirmed that appliance design significantly influences biologic response. Continuous force systems like conventional brackets elicited the highest biochemical activity, followed by the moderated responses of self-ligating brackets, and the lowest magnitude of change with the intermittent forces of clear aligners[6,13,19]. This supports the concept that lighter, intermittent forces can achieve efficient tooth movement while minimizing excessive tissue reactions[19].

The clinical implications are that GCF analysis of ALP and CTSB can serve as a valuable tool for biologic monitoring and optimizing force systems. Appliance selection should consider the desired biologic response, with conventional brackets for robust remodeling and aligners for moderated responses. The phase-specific biomarker patterns can also inform treatment timing and force adjustments. While this study has limitations, including a small sample size and short duration, it provides a foundation for future research to correlate biomarker levels with clinical parameters and investigate a wider range of molecular markers.

5. CONCLUSION

Within the limitations of this study, orthodontic tooth movement was associated with significant alterations in gingival crevicular fluid alkaline phosphatase and cathepsin-B levels, with distinct patterns observed across different appliance systems. Conventional preadjusted edgewise appliances elicited the highest elevation in both biomarkers, reflecting sustained osteoblastic activity and pronounced osteoclastic resorption throughout treatment. Self-ligating brackets demonstrated significant but moderated enzymatic responses, while clear aligner therapy exhibited the lowest biomarker elevation with an initial rise followed by stabilization, consistent with intermittent force application.

The phase-specific peak in cathepsin-B levels during early and mid-treatment followed by a subsequent reduction indicated active osteoclastic remodeling transitioning toward periodontal stabilization. Intergroup comparisons confirmed statistically significant differences among the three modalities, leading to rejection of the null hypothesis. These findings demonstrate that orthodontic appliance design significantly influences the biochemical cascade of bone remodeling, providing a biologic rationale for appliance selection based on desired tissue responses and treatment objectives.

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