Keywords
Platelet rich fibrin-Vitamin D3-Implant – ISQ- Osseointegration.

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Synergistic Impact of Vitamin D3 and PRF on Peri-Implant Outcomes in Dental Implant Placement:A 12-Month Randomized Controlled Trial.

ABSTRACT

Objective: The purpose of the paper was to study the influence Background/Purpose:A biological process known as osseointegration,in which a direct structural and functional connection is formed between the dental implant's surface and living bone,is essential to the success of dental implants.This randomized controlled trial assessed the immediate dentalimplant success rates of vitamin D3 alone versus vitamin D3 plus platelet-rich fibrin (PRF),by comparing both interventions to routine implant placementwithout adjunctive therapy.

MaterialsandMethods:The study included a total of 45 randomly assigned patients who received immediate implants placement to one of three groups: Group 1(PRF+vitamin D3), Group 2 (vitamin D3 only), or Group 3 (control).Radiographic bone density, soft tissue health (bleeding index, probing depth),and implant stability (ISQ) were evaluated at baseline, three, six, and twelvemonths. The Kruskal-Wallis test ($p<0.05$) was used for the statistical analysis.

Results: The PRF+vitamin D3 group had mean differences of 8–12 ISQ units compared to controls by 12 months, and their ISQ values were considerably higher than those of the other two groups at all intervals($p<0.01$).Additionally, this group showed better probing depths and lower bleeding ratings compared to control. In every metric, the controls performed the worst, whilethe vitamin D3-only group improved in a Moderate level.

Conclusion: In comparison to mono therapies or conventional procedures, the synergistic combination of PRF and vitamin D3 significantly enhanced peri-implant tissue health, osseointegration, and rapid implant stability. Theseresults provide support to the regular clinical application of this combinedstrategy to maximize rapid implant results. Future research should focus on cost-effectiveness and long-term (>5 years) survival rates.

Keywords:Platele rich fibrin-VitaminD3-Implant–ISQ-Osseointegration.

INTRODUCTION

Dental implantology, which provides a very reliable and efficient way to replace lost teeth, has completely transformed the field of restorative dentistry (Waghmare et al., 2024) When compared to conventional prosthetics, dental implants offer better functional and aesthetic results, greatly enhancing patients quality of life (Elani et al., 2018) A biological process known as osseointegration, in which a direct structural and functional connection is formed between the implant's surface and livingbone, is essential to the success of dental implants (Alghamdi& Jansen, 2020; Parithimarkalaignan & Padmanabhan, 2013)The firm attachment of theimplant within the jawbone is the result of thiscomplex process, which involves a complexinteraction of cellular and molecular events (Cooper&Shirazi, 2022). Although dental implants havebeenshown to have high success rates, usually between90% and 98% over a 10-year period, a number of factors can affect their stability and long-term survival (Thiebot et al., 2022)These variables include post-operative care, surgical technique, implant design, local bone quality and quantity, and systemic diseases that impact the patient (Raikar etal., 2017; Takefuji, 2025)For implant results to be effective and predictable, these factors must be optimized.In order to improve overall predictability and shorten the time to prosthesis loading, recent developments in biomaterials and regenerative techniques have concentrated on optimizing the osseointegration process and speeding bone healing (De Pace et al., 2025; Walter et al., 2022) Because of their biological characteristics that support bone metabolism and tissue regeneration, vitamin D and platelet-rich fibrin (PRF) have attracted a lot of attention among the several adjunctive therapies investigated (Farmani et al., 2021) Growth factors, cytokines, and leukocytes are abundant in PRF, an autologous blood concentrate, and are essential for angiogenesis, osteogenesis, and wound healing(Guan et al., 2023)

Rapid tissue repair and regeneration at the implant site are made possible by its three-dimensional fibrin matrix, which acts as a natural scaffold for cell migration and proliferation (Cortese et al., 2016; Hafez et al., 2015) PRF has been shown in clinical investigations to be effective in improving soft tissue healing around dental implants, encouraging the production of new bone, and increasing implant stability (Gaur et al., 2022)

It is commonly recognized that vitamin D, a fat-soluble steroid hormone, plays a crucial role in bone metabolism and calcium and phosphate balance (Buzatu et al., 2024) By regulating osteoblast differentiation, bone mineralization, and immune responses at the implant-bone interface, vitamin D affects osseointegration in addition to its systemic effects (Werny et al., 2022)

While a vitamin D shortage has been recognized as a possible risk factor for implant failure, adequate levels have been linked to better bone repair and increased implant stability (Al-Quisi et al., 2024; Cheng et al., 2024; Mohsen et al., 2024).

Even though there is a well-established individual benefitofPRFand vitamin Din dentalimplantology, there has been a growing interest in the potential synergy of the combined use of PRF and vitamin D. Amorethoroughandefficient strategyforimproving implant success is thought to be possible bytargeting both systemic (Vitamin D) and local (PRF) factors thataffectbonehealingand tissue regeneration.This combination strategy wouldresult inbetter long-term outcomes of dental implants, better soft tissue health, quicker and stronger osseointegration.

Aim of the study: The aim of this study was toassess the effect of vitamin D alone, vitamin D with fibrin-rich platelets in comparison to control on delayed implant success rate.

Materialandmethods

Studydesign,groups,andethicalconsiderations

This study employed a randomized controlled trial (RCT) design. The study was carried out at the "UniversityofAlMaarif,Iraq'sFacultyofDentistry's outpatient dental clinic". The Helsinki Declaration and the institutional research committee's ethical guidelines were followed in all procedures involving humansubjects.Toreduceselectionbias,45 adult patients were divided into three equal groups at random (n=15 each group) using a computer-generated sequence. Group 3 was the control group, undergoing routine implant insertion without any extra procedures, whereas Group 1 received PRF in addition to Vitamin D3. Group 2 received VitaminD3alone.Over a12-monthfollow-upperiod,clinical and radiographic examinations were conducted to evaluate the results.

Samplesizecalculation

To determine if the Group 2 (treatment) mean (μ2) differs from the Group 1 (reference) mean (μ1), a parallel two-group design was used. A two-sided,two-sample Z-test with a Type I error rate (α) of 0.05 was used for the comparison.It is assumed that the standard deviations for Groups 1 and 2 are 6 and 5, respectively.The re-estimated target sample sizesare N1 = 14 subjects for Group 1 and N2 = 14subjectsforGroup2,assumingamean ISQ difference (δ = μ2 - μ1) of 80.9 - 74.9 = 6 inorder to achieve a conditional power of 80%. The samplewasincreasedto15participantsineachgroup. PASS 2025, version 25.0.2, was used to re-estimate the intended sample size.

EligibilityCriteria

Adult patients(> 18years)whowere ingoodgeneral

health, did not smoke, had enough bone volume for an immediate implant insertion, and gave their informedconsentwerealleligible.Patientsoutsideof the designated age range, smokers and people with medically compromised conditions such as thosewith uncontrolled diabetes mellitus, hypertension, osteoporosis, or immunocompromised conditions were excluded based on exclusion criteria. Also, pregnant or breastfeeding women were excluded.

EquipmentandMaterials

Inadditiontocommercially puretitanium ortitanium alloy (Ti-6Al-4V) implants of specified dimensions, the study used high-dose vitamin D3 powder (10,000 IU)applieddirectly totheimplantsite.Sterilesingle-use carbon steel surgical bladeswere used for aseptic incisions, and reverse-cutting suture needles and polypropylene suture material were used for accurate flap closure. To prepare PRF, 9 mL of venous blood was drawn from the antecubital vein and placed in glass-coated plastic tubes without anticoagulants. A PC-02 centrifuge was then used to centrifuge the blood for 12 minutes at 2,700 rpm. A PRF compression box was used to compress the resultant fibrin clot into a membrane, while the serum waskept for therapeutic application.

Treatmentprotocol

After venipuncture, blood samples were centrifuged right away to separate the fibrin clot, which was subsequently compressed into a membrane as part of the PRF preparation procedure. A crestal incisionwas made and a full-thickness mucoperiosteal flap was raised during the surgical procedure. In order to prevent heat necrosis, a consistent drilling sequence was performed under saline irrigation after preoperative CBCT imaging evaluated ridge height and bone quality.

MethodsofEvaluation

At three and six months after implant placement, clinical evaluations included the Modified Sulcus Bleeding Index (MSBI), which has ratings ranging from 0 (no bleeding) to 3 (severe bleeding).

To evaluate peri-implant health, Probing PocketDepth (PPD) was assessed at three and six months. Resonance frequency analysis (RFA) was used to measure implant stability. Implant Stability Quotient (ISQ) measurements were obtained at6(T1),12(T2), and immediately post-placement (Tx), as well as following prosthesis loading (T0). The stability ofISQ readings was classified as low (<60), medium (60–69), or high (>70). Preoperative and 12-month CBCT scans were used for radiographic evaluationsin order to assess bone density and osseointegration(Gupta, 2022) Panoramic radiographs were taken at 3, 6, and 12 months totrack the growth of trabecular bone.

StatisticalAnalysis

Toascertaintheeffectivenessofthetherapies,data gathered from clinical and radiographic evaluations werestatisticallyanalyzed,usingthe“Kruskal-Wallis test”.“GraphPadPrism” wasused tographically and statistically compare the three groups.

Results

The study enrolled a total of 45 participants, who were equally divided into three groups: Vitamin D plusPRF(Group1),VitaminDonly(Group2), and Control(Group 3), witheach groupconsistingof 15 participants (33.3%). The demographic characteristicsoftheparticipantsaresummarized inTable1.Themeanageofthecohortwas33.6± 5.9 years, with a median age of 32.0 years. A gender imbalance was observed, with males constituting the majority (64.4%) and females accounting for 35.6% of the study sample. The Implant Stability Quotient (ISQ)medianonthebuccalsidewas80.0 (range: 70.0–91.0). With a mean of 77.9 ± 6.1 and a medianof75.0,thelingualsideshowedsomewhat less stability. With a mean of 1.2 ± 0.62 and a median of 1.0 (range: 0–2.0), the Bleeding Index indicatedhealthyperi-implanttissuesandless gingival inflammation. Likewise, Probing Depth (PD) values range from 3.0 to 4.0 mm and have a mean of 3.4±0.49mmandamedianof3.0mm.

Implant Stability Quotient (ISQ) Measurements at buccal and lingual sites

InitialStability: Theinitialimplant stability, assessed using the Implant Stability Quotient (ISQ) at buccal and lingual sites, revealed no statistically significant differences among the groups; the groups ISQ values were comparable at baseline (Figure 1A, 2A).

At 3 Months: The PRF plus Vitamin D group had much higher values of ISQ at compared with other groups. This pattern indicates that the combined treatment can hasten bone repair and enhance the secondary stability in the critical early phase of the process of osseointegration (Figure 1B, 2B).

At 6 Months: The PRF plus Vitamin D group exhibitedthe highest stability advantage, whereasthe Vitamin D-only group showed moderate stability,and the control group was the one that depicted the lowest values of the ISQ. These findings suggest that the positive effects of PRF supplementation are not limited to the first healing phase (Figure 1C, 2C).

At12Months:Implantstreatedwiththiscombination showed the highest ISQ values, confirming the long-term stability of these implants. Conversely, the controlgroup had the lowest desirableresults (Figure 1D, 2D).

BleedingIndex

An indicator of gingival inflammation, the bleeding index, was compared in the groups. The PRF and Vitamin D grouprecorded the lowestbleeding scores, which implies an enhanced peri-implant soft tissue health and a decreased inflammatory reaction. The controlgroup,however,hadthehighestbleeding

index, which could be due to a higher susceptibilityto the condition of peri-implant mucositis without adjunctive treatments. The results of the Vitamin D-only group were intermediate (Figure 3).

ProbingDepth(PD)Measurements(Figure4)

At 3 Months (Figure 4 A): PRF plus Vitamin Dgroup showed significantly lower probing depthsthan the other groups, which pointed to reduced inflammation of the peri-implant area and improved adaptation of the soft tissues.

At 6 Months (Figure 4B): The probing depths were consistently lower in the PRF plus Vitamin D group, and were greater in the control group, which hints at increasing peri-implant tissue breakdown. The Vitamin D only condition once again showed intermediate outcomes.

Discussion

Inafocusonthelevel ofsuccessofimmediate dental implants, the present study aimed at determining the effect of vitamin D3 and platelet-rich fibrin (PRF), used separately and in combination, on the success rate of immediate dental implants. The most significant result was that, compared to vitamin D3 alone or a control group, PRF and vitamin D3 combination significantly enhanced implant stability and promoted the health of soft tissues.

To ensure the success of the process of osseointegration, vitamin D is vital in calcium homeostasis and bone metabolism. The results of the study, which indicated that the vitamin D-only group had moderate improvements, are consistent with previous studies that suggest that adequate vitamin D levels promote bone growth around dental implants, hence speeding up bone repair(Ayyad et al., 2025; Buzatu et al., 2024) Vitamin D's effects on bone remodeling are mediated by vitamin D receptors (VDRs) in bone cells, which promote osteoblast development and mineralization through a variety of biochemical pathways (Li et al., 2023; Nakamichi et al., 2018; van Driel & van Leeuwen, 2023; van Driel & van Leeuwen, 2014) The immunomodulatory properties of vitamin D are further highlighted since they decrease inflammation at the implant site (Buzatuetal.,2024;Markopoulosetal.,2021;Tallon et al., 2024; Vesala & Dontas, 2020) However, the investigations also highlighted the significance of optimal rather than overly high levels of vitamin D, warning against the possible negative effects of excessive levels (hypervitaminosis D) (Cheng et al., 2024; Marcinowska-Suchowierska et al., 2018) It is recommended that future studiesbe conducted onthe best dosage and delivery strategies.

PRF, an autologous blood concentrate, is known foritsrestorativequalities(Chouetal.,2020;Mironetal., 2017) It is rich in growth factors, cytokines, and leukocytes necessary for tissue healing, angiogenesis, and osteogenesis(Baca-Gonzalez et al., 2022) Given that the PRF with Vitamin D group continuously shownbetterresultsinimplantstabilityandsoft tissue health, the study provides compelling evidence for PRF's effectiveness. PRF has been shown in previous studies to have a significant effect on the healing of soft tissues, reducing peri-implant inflammation and increasing soft tissue adaptations (Kosmidis et al., 2023; Strauss et al., 2020; Wong et al., 2021) In accordance with its anti-inflammatory effects, PRF also has a significant effect on the healing of soft tissues, reducing peri-implant inflammation and increasing soft tissue adaptations (Tawfik, 2016)

The most significant finding is that vitamin D3 and PRF act in conjunction to produce consistently better results insoft tissue healthand implant stability. This synergy is due to their complementary mechanisms. PRFprovidescues for tissue regeneration at the local level in the form of biological factors and a physical matrix, while vitamin D provides cues for bone healing at a system level. (de Lima Barbosa et al., 2023) Both strategies will help achieve better soft tissue health and accelerate and strengthen osseointegration, which is the key to peri-implantitis prevention (Smeets et al., 2022; Yi et al., 2022). Combined use of these two is still in its infancy but thisstudyprovidesgoodevidenceoftheirtherapeutic benefits and a more holistic approach.

Some of the limitations that may limitgeneralizability include the sample size. Future studies should involve larger cohorts, histological examination, the success of bone grafting, delayed implant placement, effects over a longer period of time beyond a year, and the optimization of vitaminD dosages and preparation methods for PRF. Other recommendations include cost-effectiveness assessments and individual treatment strategies.

Conclusion:

The results show that vitamin D3 and PRF showgreat potential in increasing the success rate of immediate implant placement. The combination results in better osseointegration, long term stability, andbettersofttissuehealth indicators.Thestudyalso highlights the safety and feasibility of PRF applications and preoperative vitamin D level evaluation as low-risk methods to enhance osseointegration and implant success.

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Ethical statement

The authorsdeclarethat the Helsinki Declaration and the institutional research committee's ethical guidelines were followed in all procedures of the study. An informed consent was signed by the participants of the study.

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Table1:Baselinecharacteristicsofthestudyparticipants

Descriptivecharacteristics	**No.(%)**
Groups	
Vit.DplusPRF(Group1)	15(33.3%)
Vit.Donly(Group2)	15(33.3%)
Control(Group3)	15(33.3%)
Age(Years)	
Mean±SD	33.6±5.9
Median(Min.-Max.)	32.0(25.0-43.0)
Gender	
Male	29(64.4%)
Female	16(35.6%)
ISQbuccal	
Mean±SD	79.18±5.4
Median(Min.-Max.)	80.0(70.0-91.0)
ISQlingual	
Mean±SD	77.9±6.1
Median(Min.-Max.)	75.0(70.0-91.0)
BI	
Mean±SD	1.2±0.62
Median(Min.-Max.)	1.0(0-2.0)
PD(mm)	
Mean±SD	3.4±0.49
Median(Min.-Max.)	3.0(3.0-4.0)

SD: Standard deviation PRF: Plasma rich fibrin Min.: Minimum Max.: Maximum

ISQ: Implant Stability Quotient BI: Bleeding index PD: Probing depth mm:millimeters

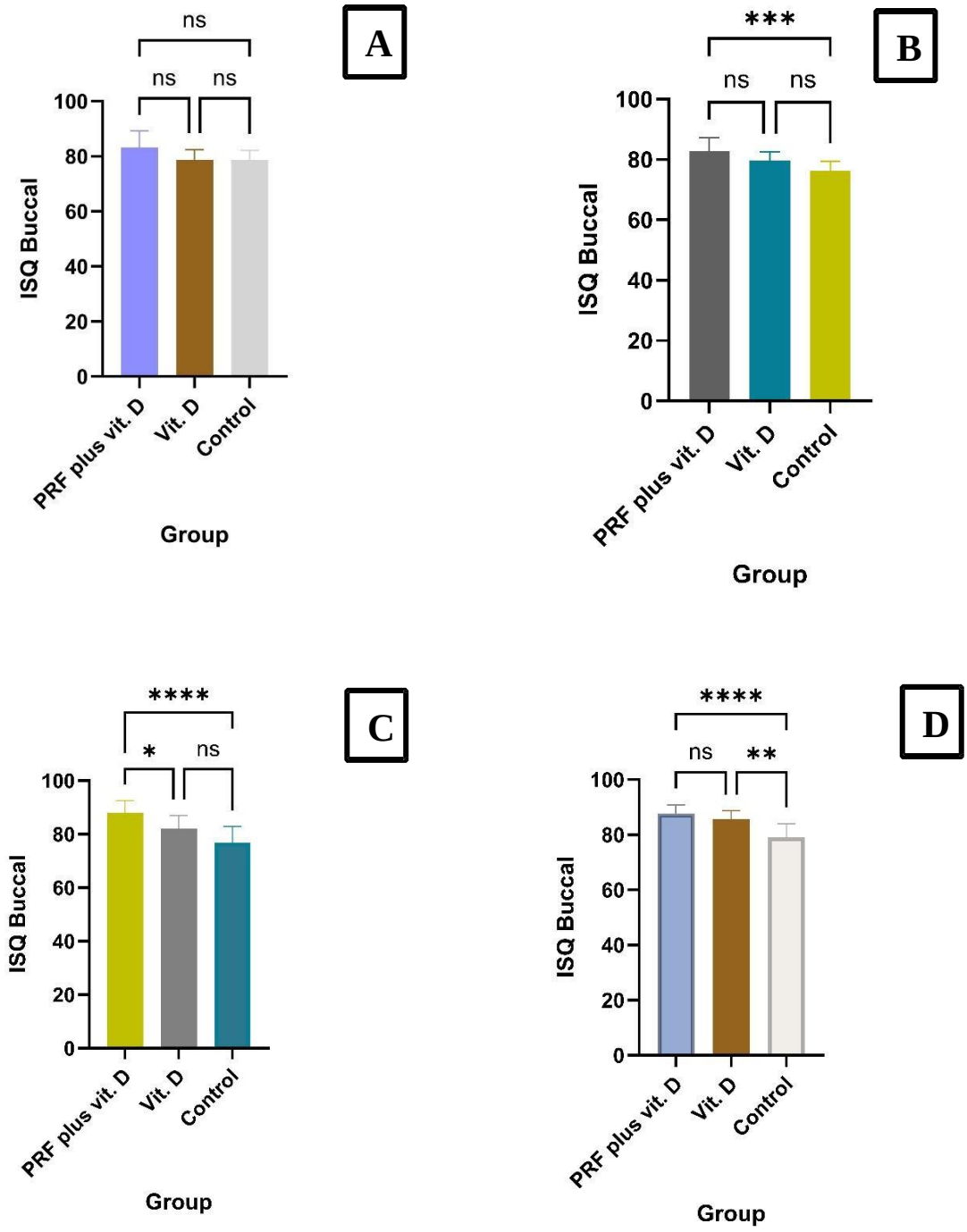

Figure 1: Comparison between the study groups regarding buccal implant stability quotient (ISQ) (A: initial, B: 3 months, C: 6 months, D: 12 months)

ns:Non-significant *<0.05:statisticallysignificant ***<0.001:Highlysignificant

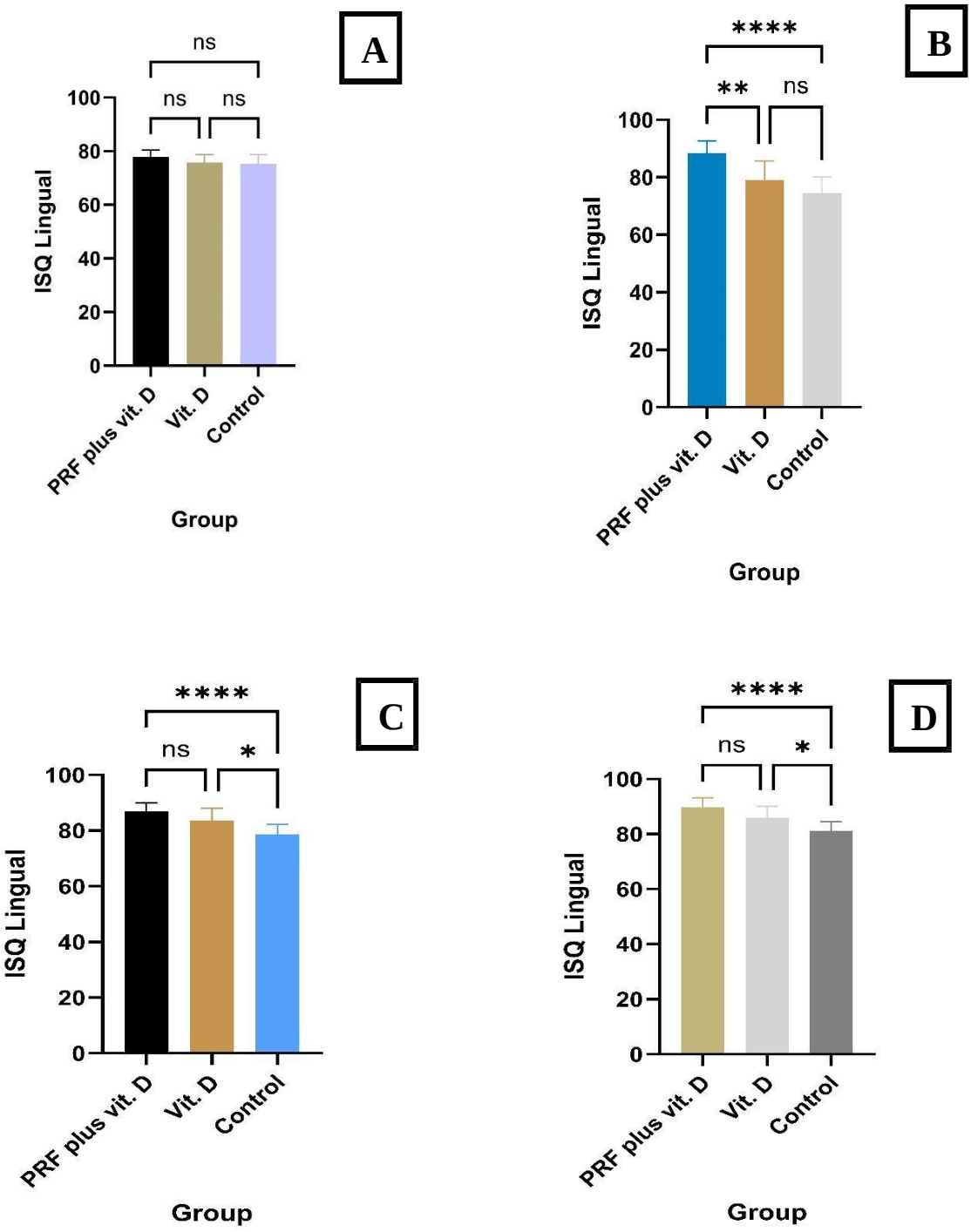

Figure2:Comparisonbetweenthestudygroupsregardinglingualimplantstabilityquotient(ISQ)(A:initial, B: 3 months, C: 6 months, D: 12 months)

ns:Non-significant *<0.05:statisticallysignificant ***<0.001:Highlysignificant

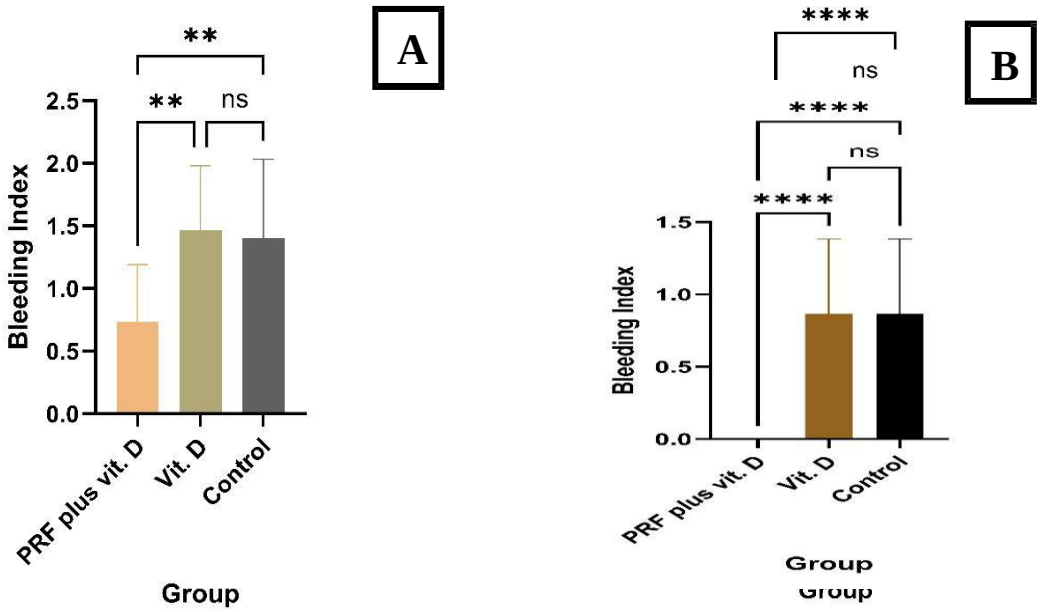

Figure3:Comparisonbetweenthestudygroupsregardingbleedingindex(BI)(A: After3months,B:After6 months)

ns:Non-significant **Statisticallysignificant<0.05 ***highlystatisticallysignificant<0.001

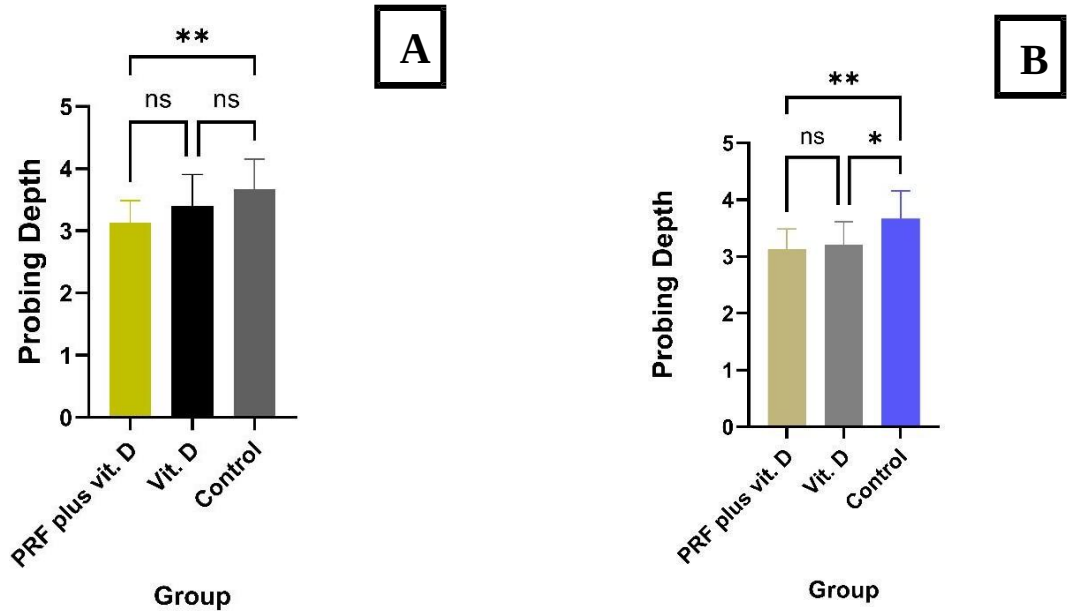

Figure4:Comparisonbetweenthestudygroupsregardingprobingdepth(PD) (A:After3months,B:After6 months)

ns:Non-significant *Statisticallysignificant<0.05