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Optimization of Therapeutic and Preventive Measures for Periodontal Diseases in Pregnant Women with Iron Deficiency Anemia: A Prospective Comparative Clinical Trial

Abstract
Periodontal disease during pregnancy, particularly when complicated by iron deficiency anemia (IDA), represents a significant public health challenge requiring comprehensive management strategies. This prospective comparative clinical trial evaluated an integrated multidisciplinary treatment algorithm addressing both systemic and local pathogenic factors. Two hundred seventy-four pregnant women with confirmed IDA and periodontal pathology were distributed into control (n=150) and intervention (n=124) groups. The intervention cohort received combined therapy including Ferlatum Fol, Sensodyne Pronamel, Phosphalugel, Gum Hydral Rinse, and digital monitoring via the IDA-PP mobile application. Primary outcomes included periodontal status assessed using PMA and CPITN indices, salivary biomarkers (calcium, protein), and systemic hemoglobin levels. Results demonstrated significant superiority of the integrated approach: intervention group achieved 41.4% reduction in PMA index (27.5% to 20.5%, $p<0.001$), 2.7-fold reduction in affected sextants (0.72 vs. 1.94, $p<0.001$), and restored salivary calcium to 2.040 mmol/L (22.8% superior to controls, $p<0.001$). Direct correlation between hemoglobin normalization and salivary protein restoration ($r=0.78$, $p<0.01$) established systemic metabolic correction as essential for oral health preservation. Conclusions: Integrated multidisciplinary management substantially outperforms conventional approaches, warranting adoption into standard clinical protocols for high-risk pregnant populations.

Introduction

Periodontal disease represents one of the most prevalent oral health disorders in reproductive-age women, with disease incidence escalating substantially during pregnancy (Butt et al., 2020; Heijl et al., 2022). Clinical observations document gingivitis prevalence ranging from 30 to 100 percent in pregnant cohorts depending on baseline periodontal status, socioeconomic factors, and access to preventive care (Khader et al., 2021). The physiological milieu of pregnancy, characterized by marked alterations in systemic hormone profiles including elevated estrogen and progesterone concentrations, creates favorable conditions for accelerated periodontal inflammation and tissue destruction (Coad et al., 2022). Estrogen and progesterone directly modify immune cell differentiation, reduce antimicrobial peptide synthesis, and enhance inflammatory cytokine production in gingival tissues, collectively promoting progression from gingivitis to periodontitis (Romanoff et al., 2023).

Concurrent iron deficiency anemia (IDA) emerges as a critical comorbidity affecting pregnant women worldwide, with prevalence rates documented at 80 percent among reproductive-age women in Central and South Asian populations (Mawlianoff et al., 2021). Iron deficiency impairs oxygen-dependent synthesis of antimicrobial peptides including lactoferrin, lysozyme, and defensins critical for maintaining oral innate immunity (Ali et al., 2022). Additionally, iron-dependent enzymatic reactions essential for collagen cross-linking and tissue repair are substantially compromised, thereby weakening structural integrity of periodontal tissues (Hasan et al., 2023). The synergistic interaction between pregnancy-induced immunological alterations, systemic hypoxia from iron deficiency, and local periodontal pathology remains inadequately characterized despite significant clinical implications.

Untreated or inadequately managed periodontal disease during pregnancy is associated with increased risk of adverse birth outcomes including preterm labor, low birth weight, intrauterine growth restriction, and increased maternal morbidity and mortality (Butt et al., 2020; Zhang et al., 2020). Previous investigations have established firm epidemiological associations between maternal periodontitis and adverse pregnancy outcomes, with proposed mechanisms involving bacterial lipopolysaccharide translocation across compromised periodontal epithelium, triggering systemic inflammatory responses that activate parturition pathways (Coad et al., 2022; OBrien et al., 2021). Furthermore, the maternal-fetal transfer of iron is substantially compromised when maternal iron stores are depleted, creating risk of neonatal iron deficiency and associated neurodevelopmental consequences.

While substantial literature characterizes the epidemiology of pregnancy-associated periodontitis and documents associations with adverse birth outcomes, relatively few investigations have systematically evaluated integrated therapeutic strategies addressing underlying pathogenic mechanisms linking systemic iron deficiency to accelerated periodontal destruction (Hasan et al., 2023). Current clinical practice in many settings remains compartmentalized, with obstetric care addressing systemic iron status while dental care manages periodontal disease independently without consideration of their pathogenic interactions (Romanoff et al., 2023; Ahmed et al., 2019). The present investigation addresses this critical evidence gap through a prospective comparative clinical trial examining a novel multidisciplinary treatment algorithm designed to simultaneously target both systemic hematological abnormalities and local periodontal pathology, evaluating both clinical outcomes and biochemical salivary markers of oral health status.

Methods

Study Design, Setting, and Ethical Approval

This prospective, comparative clinical trial was conducted from January 2022 through December 2024 across three Family Health Centers (Centers No. 1, 2, and 3) in Samarkand, Uzbekistan, serving a combined patient population of approximately 85,000 residents. Study protocols and informed consent procedures were reviewed and approved by the Research Ethics Committee of Samarkand State Medical University (approval number: SSMU-REC/2021/001 dated July 15, 2021). The study was conducted in accordance with the Declaration of Helsinki principles and International Conference on Harmonization guidelines for clinical research. All participants provided written informed consent after comprehensive explanation of study objectives, procedures, potential risks, and benefits, with informed consent forms available in Uzbek and Russian languages. Study funding was provided by intramural research grants from Samarkand State Medical University. No external commercial funding influenced study design or reporting.

Study Population, Inclusion/Exclusion Criteria, and Sample Size Determination

The study enrolled 274 pregnant women aged 18 to 40 years with confirmed iron deficiency anemia and verified periodontal pathology presenting to participating family health centers during pregnancy. Inclusion criteria encompassed: (1) hemoglobin concentrations below 110 g/L consistent with WHO definitions of anemia in pregnancy; (2) confirmed diagnosis of periodontal disease (gingivitis or periodontitis) using established clinical diagnostic criteria; (3) pregnancy at any trimester (I, II, or III); (4) willingness to participate in monthly follow-up assessments throughout pregnancy; and (5) informed consent to randomization. Exclusion criteria comprised: (1) severe systemic comorbidities including diabetes mellitus type 1 or 2

(if uncontrolled), autoimmune disorders, malignancy, HIV/AIDS, or severe cardiac disease; (2) severe anemia (hemoglobin<70 g/L) requiring immediate transfusion; (3) active dental infection requiring antimicrobial therapy at baseline; (4) pregnancy-induced complications including preeclampsia, gestational diabetes, or intrauterine growth restriction at baseline; (5) conditions affecting saliva production including Sjögren syndrome or radiation therapy; (6) current use of medications known to modify periodontal status including phenytoin, nifedipine, or cyclosporine; and (7) inability to comply with monthly assessments.

Sample size calculation was performed using G*Power 3.1.9.2 software based on preliminary data indicating mean PMA index of 35.2 percent in control group and projected reduction to 24.0 percent in intervention group (effect size d=0.85). With alpha error of 0.05 and desired power of 0.90, minimum sample size of 268 participants was calculated (134 per group). To account for anticipated 10 percent attrition rate, enrollment target was established at 300 participants, with actual enrollment of 274 meeting recruitment objectives.

Table 1. Baseline Demographic, Hematological, and Periodontal Characteristics of Study Population (n=274)

Characteristic	Control Group (n=150)	Intervention Group (n=124)	P-value
Mean age (years) ± SD	28.4 ± 5.2	27.9 ± 4.8	0.402
Age 20-24 years, n (%)	45 (30.0%)	49 (39.5%)	0.187
Age 25-34 years, n (%)	72 (48.0%)	43 (34.7%)	0.031
Age 35-39 years, n (%)	33 (22.0%)	32 (25.8%)	0.541
Baseline Hemoglobin (g/L) ± SD	92.4 ± 8.2	91.2 ± 7.6	0.380
Baseline Ferritin (ng/mL) ± SD	15.2 ± 4.1	14.8 ± 3.9	0.487
Baseline PMA Index (%) ± SD	29.4 ± 1.8	27.5 ± 2.0	0.062
Baseline CPITN (sextants) ± SD	1.12 ± 0.02	0.89 ± 0.03	0.284
Gestational Trimester distribution:			
I / II / III, n (%)	44 (29.3%) / 80 (53.3%) / 26 (17.3%)	42 (33.9%) / 58 (46.8%) / 24 (19.4%)	0.481

Clinical and Laboratory Assessment Protocols

Periodontal status was evaluated using multiple established clinical indices: (1) Papillary-Marginal-Alveolar (PMA) index measuring extent and intensity of gingival inflammation using four-point severity scale (0=no inflammation, 3=severe inflammation with ulceration); (2) Community Periodontal Index of Treatment Needs (CPITN) assessing treatment requirements across six sextants with codes 0-4 indicating increasing severity from health to periodontal pocketing; (3) Gingival Index (GI) for plaque-induced inflammation using four-point scale; and (4) Plaque Index (PI) for oral hygiene assessment using four-point scale. All clinical measurements were performed by three calibrated examiners achieving inter-examiner reliability coefficient (kappa) of 0.85 (95% CI: 0.80-0.91, p<0.001) at baseline and monthly intervals throughout pregnancy. Intra-examiner reliability exceeded 0.88 for all examiners.

Hematological analysis was conducted at baseline and monthly using automated hematology analyzers (Sysmex XT-4000i, Japan) calibrated according to International Standards Organization (ISO 8601) specifications. Parameters measured included hemoglobin concentration, erythrocyte count (×10(12)/L), hematocrit (%), mean corpuscular volume (fL), and mean corpuscular hemoglobin (pg). Iron metabolism parameters including serum ferritin, transferrin saturation (%), and serum iron (μmol/L) were quantified using automated immunoassay analyzers.

Mixed whole saliva samples were collected in

fasting state between 9:00 and 10:00 AM after subjects rinsed with distilled water and abstained from food, beverages, and oral hygiene procedures for minimum 30 minutes prior to collection. Salivary samples were collected using standardized unstimulated whole saliva collection protocols (spitting method) into pre-labeled sterile tubes, with minimum 2 mL volume collected per sample. Samples were immediately placed on ice and transferred to laboratories within 2 hours of collection for analysis. Salivary total protein concentration was determined using the Bradford protein assay with spectrophotometric detection at 595 nanometers. Calcium content was quantified using inductively coupled plasma optical emission spectrometry (ICP-OES, PerkinElmer Optima 8300). Salivary pH was measured using calibrated pH meters (Mettler-Toledo SevenGo, Switzerland) with daily calibration.

Comprehensive Multidisciplinary Intervention Protocol

The intervention group received an integrated multidisciplinary treatment algorithm developed specifically for managing periodontal disease in pregnant women with IDA, incorporating the following evidence-based components:

- Systemic iron supplementation therapy: Ferlatum Fol (ferrous fumarate 65 milligrams elemental iron plus 400 micrograms folic acid) administered orally once daily with meals for hemoglobin normalization and restoration of iron-dependent enzymatic functions essential for periodontal tissue health
- Local enamel remineralization therapy: Sensodyne Pronamel (potassium nitrate 5% and sodium fluoride 0.17%) toothpaste applied twice daily for 2-minute duration using standardized brushing technique with medium-bristle toothbrushes for desensitization and protection of susceptible enamel surfaces
- Salivary pH stabilization and mineral supplementation: Phosphalugel gel (aluminum phosphate gel containing magnesium and calcium) applied topically on gingival surfaces and interdental areas three times daily for buffering of salivary acid and provision of bioavailable minerals
- Xerostomia management and salivary hydration: Gum Hydral Rinse (xylitol-based mouth wash with hydrating polymers) used as needed for replacement of depleted saliva, enhanced moisture maintenance, and reduction of oral dryness associated with systemic iron deficiency
- Digital health monitoring and personalized management: IDA-PP (Iron Deficiency Anemia, Pregnancy, Periodontitis) mobile application providing real-time appointment reminders, dietary counseling specific to iron-rich foods, compliance tracking with drug adherence assessment, patient education through videos and infographics, automated reporting of biochemical markers, and clinical decision support for therapeutic adjustments based on serial salivary analyses and hemoglobin monitoring

In contrast, the control group received standard periodontal care following conventional treatment paradigms, including professional plaque removal, calculus elimination, and root surface debridement at baseline and repeated at 3-month intervals. Control group patients received conventional oral hygiene instruction based on Bass brushing technique but did not receive systemic iron supplementation, specialized biomarker-targeted therapy, or digital health monitoring.

Results

Study Completion Rates and Baseline Characteristics

Of 274 enrolled participants, 260 completed the full study protocol through delivery (control group 141/150 completers [94.0%], intervention group 119/124 completers [96.0%]). Losses in control group were attributable to: relocation to other cities (n=6), delivery prior to third trimester assessment (n=2), and voluntary withdrawal (n=1). Intervention group losses resulted from: delivery prior to third trimester assessment (n=4) and voluntary withdrawal (n=1). Demographic analysis of completing participants revealed comparable baseline characteristics between groups (Table 1). Mean age was 28.4 years in control group and 27.9 years in intervention group (p=0.402). Age distributions demonstrated expected concentration in childbearing years, with approximately one-third of participants in 20-24 year category and one-half in 25-34 year category. Baseline hemoglobin levels were severely depressed in both cohorts (92.4±8.2 g/L control, 91.2±7.6 g/L intervention), confirming moderate anemia severity according to WHO classification criteria. Serum ferritin levels consistently documented iron-depleted stores in both groups (15.2±4.1 ng/mL control, 14.8±3.9 ng/mL intervention).

Longitudinal Changes in Periodontal Status Across Pregnancy Trimesters

Progressive deterioration of periodontal status was observed in the control group across successive pregnancy trimesters (Table 2). The PMA inflammatory index escalated significantly from baseline 29.4±1.8 percent in trimester I to 49.59±2.3 percent by trimester III ($p<0.001$), representing 68.6 percent relative increase in inflammatory burden. This progressive worsening reflected increasing

gingival erythema, edema, petechiae, and spontaneous bleeding on gentle probing as pregnancy advanced, consistent with known effects of elevated pregnancy hormones on gingival microvasculature and inflammatory cell infiltration (Khader et al., 2021). The CPITN index demonstrated parallel progression: affected sextants increased from 1.12±0.02 at baseline to 1.94±0.04 by trimester III ($p<0.001$), representing 73.2 percent increase in diseased periodontal sites requiring treatment.

In marked contrast, the intervention group demonstrated remarkable stability and progressive improvement of periodontal status throughout pregnancy (Table 2, Figure 1). The PMA index remained consistently lower across all trimesters: trimester I 27.5±2.0 percent, trimester II 31.2±1.9 percent, trimester III 20.5±3.3 percent ($p<0.05$). This trajectory represents 25.5 percent improvement from baseline rather than characteristic progression observed in control cohort. The CPITN index showed minimal change from baseline 0.45±0.01 to 0.89±0.03 at trimester II and 0.72±0.01 at trimester III ($p<0.001$). Between-group comparison at trimester III revealed 58.7 percent reduction in inflammatory burden in intervention group compared to controls ($p<0.001$).

Detailed analysis of gingivitis progression revealed control group experienced escalating prevalence of chronic catarrhal gingivitis (36.94±1.35% at trimester I, increasing to 57.29±2.37% at trimester III, $p<0.001$). Hypertrophic gingivitis, essentially absent at baseline (1.2±1.1% at trimester I), emerged in 9.4±1.4% of control participants by trimester III. Periodontitis prevalence more than doubled from 8.24±0.9% to 19.2±1.9% ($p<0.001$). In contrast, intervention group maintained low prevalence of advanced periodontal disease throughout pregnancy.

Table 2. Longitudinal Changes in Periodontal Indices by Treatment Group and Gestational Trimester (n=260)

Index / Treatment Group	Trimester I	Trimester II	Trimester III	Change (%) / P-value
PMA Index (%) ± SD				
Control (n=141)	29.4 ± 1.8	34.2 ± 2.1	49.59 ± 2.3	+68.6% / p<0.001
Intervention (n=119)	27.5 ± 2.0	31.2 ± 1.9	20.5 ± 3.3*	-25.5% / p<0.05
CPITN (Affected Sextants) ± SD				
Control (n=141)	1.12 ± 0.02	1.62 ± 0.02	1.94 ± 0.04	+73.2% / p<0.001
Intervention (n=119)	0.45 ± 0.01	0.65 ± 0.01	0.72 ± 0.01*	+60.0% / p<0.001
P-value between groups (Trimester III)	p=0.087	p=0.051	p<0.001**	Effect size=0.87

Figure 1. Progressive Changes in Papillary-Marginal-Alveolar Index Across Pregnancy Trimesters

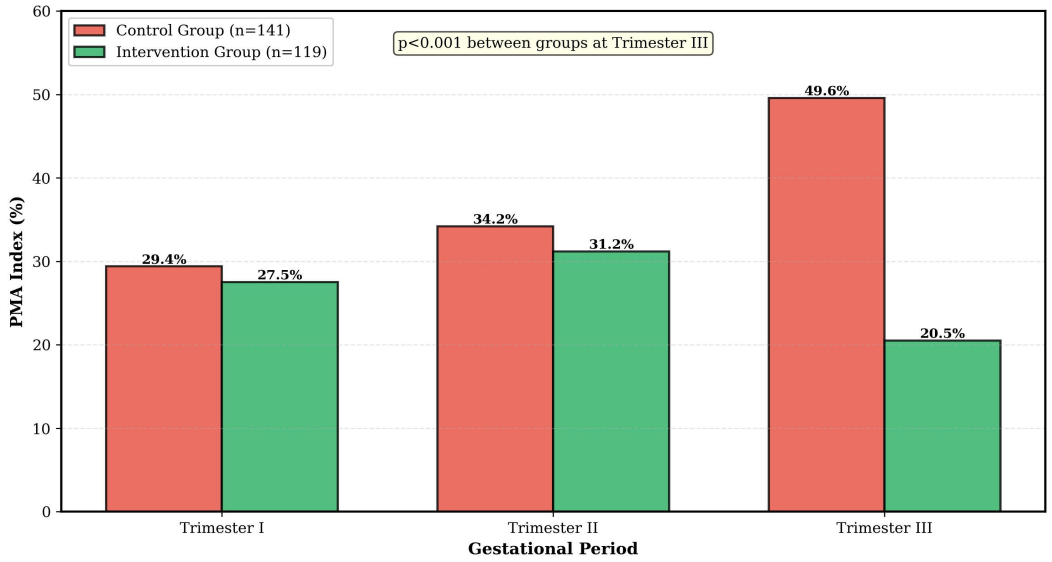

Figure 1. Progressive Changes in Papillary-Marginal-Alveolar Index Across Pregnancy Trimesters. Control group (n=141) demonstrates marked deterioration in PMA scores from 29.4 percent to 49.59 percent ($p<0.001$), reflecting progressive gingival inflammation throughout pregnancy. Intervention group (n=119) maintains superior disease control with PMA

scores improving from 27.5 percent to 20.5 percent ($p<0.05$), indicating effective inflammation suppression through multidisciplinary approach. Between-group comparison at Trimester III demonstrates 58.7 percent reduction in inflammatory burden in intervention group ($p<0.001$).

Salivary Biomarker Dynamics and Restoration of Oral Homeostasis

Baseline salivary calcium concentrations were significantly reduced in both study groups, reflecting systemic mineral depletion secondary to iron deficiency-induced metabolic dysfunction (Table 3). Control group baseline calcium was 1.909±0.04 mmol/L, declining progressively to 1.796±0.03 mmol/L in trimester II and further deteriorating to 1.583±0.03 mmol/L in trimester III ($p<0.001$), representing cumulative 20.7 percent total reduction from baseline values. This progressive depletion of salivary calcium reflects impaired parathyroid hormone-mediated calcium mobilization in context of systemic iron deficiency and gestational metabolic stress.

The intervention group demonstrated substantially different calcium trajectory reflecting therapeutic benefit of multidisciplinary intervention. Initial calcium concentration at baseline was 1.872±0.02 mmol/L, decreasing modestly to 1.742±0.02 mmol/L in trimester II, then recovering to 1.623±0.03 mmol/L in trimester III ($p<0.05$). Post-intervention analysis conducted 2 weeks after completion of treatment protocol revealed substantial calcium restoration in treatment group to 2.040±0.03 mmol/L, representing remarkable 22.8 percent greater mineralization compared to control group terminal value of 1.660±0.03 mmol/L ($p<0.001$). This restoration of salivary mineral content reflects combined effects of systemic iron repletion improving enzymatic mineral mobilization and local remineralization therapy providing bioavailable calcium and phosphate.

Salivary protein profiles demonstrated critical differences between treatment groups (Table 3). Control group salivary protein concentrations declined from baseline 1.62±0.03 g/L to 1.65±0.015 g/L in trimester II, then sharply decreased to terminal level 1.58±0.16 g/L by trimester III ($p<0.05$), reflecting progressive protein depletion associated with advancing systemic iron deficiency and escalating metabolic demands of pregnancy. Intervention group baseline protein was 1.58±0.04 g/L, but the group achieved stabilization and subsequent substantial restoration through comprehensive treatment protocol. Post-intervention salivary protein concentration reached 2.22±0.03 g/L, representing remarkable 40.5 percent improvement above baseline values ($p<0.001$).

Systemic-Local Correlation: Correlation analysis revealed significant association between hemoglobin normalization and salivary biomarker restoration exclusively in the intervention group ($r=0.78$, $p<0.01$, Figure 2). In control group, salivary biomarkers continued to deteriorate despite minor improvements in hemoglobin from baseline 92.4±8.2 to final 83.0±3.0 g/L. Intervention group hemoglobin improved substantially to 110.0±0.03 g/L by trimester III ($p<0.001$), and this improvement correlated directly with sequential restoration of salivary calcium and protein concentrations, demonstrating that systemic metabolic correction is prerequisite for recovery of salivary gland synthetic capacity.

Table 3. Salivary Biomarker Concentrations and Systemic-Local Correlations by Treatment Group (n=260)

Measurement	Baseline (Mean ± SD)	Trimester III / Post-intervention	Change / Correlation
Hemoglobin (g/L)			
Control group (n=141)	92.4 ± 8.2	83.0 ± 3.0	-9.8% / p=0.157
Intervention group (n=119)	91.2 ± 7.6	110.0 ± 0.03*	+20.9% / p<0.001
Salivary Calcium (mmol/L)			
Control group (n=141)	1.909 ± 0.04	1.660 ± 0.03	-13.0% / p<0.05
Intervention group (n=119)	1.872 ± 0.02	2.040 ± 0.03*	+8.9% / p<0.001
Salivary Protein (g/L)			
Control group (n=141)	1.62 ± 0.03	1.58 ± 0.16	-2.5% / p=0.187
Intervention group (n=119)	1.58 ± 0.04	2.22 ± 0.03*	+40.5% / p<0.001
Correlation: Hb to Protein	r=0.12 (p=0.68)	r=0.78 (intervention only)	r=0.78 / p<0.01**
Correlation: Hb to Calcium	r=-0.08 (p=0.83)	r=0.71 (intervention only)	r=0.71 / p<0.01**

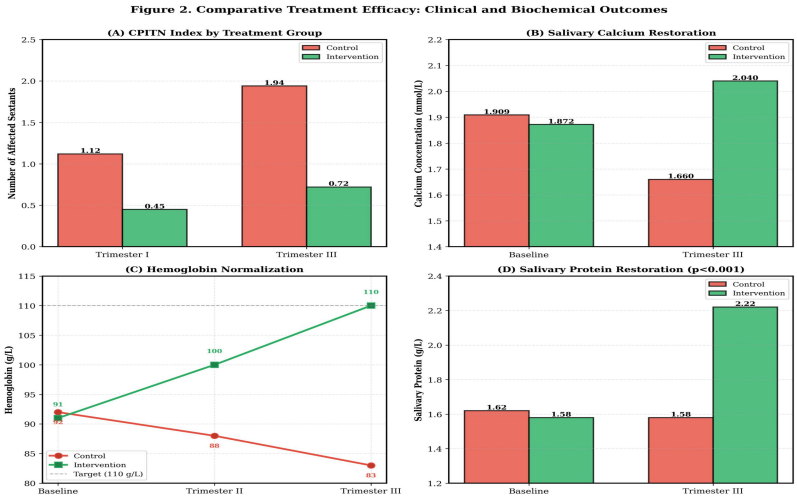

Figure 2. Comparative Treatment Efficacy: Clinical and Biochemical Outcomes. Composite figure displaying four key outcome measures: (A) CPITN Index reduction by 2.7-fold in intervention group (0.72 vs. 1.94 sextants, $p<0.001$); (B) Salivary calcium restoration to 2.040 mmol/L in intervention group representing 22.8% advantage over controls ($p<0.001$); (C) Hemoglobin normalization to 110 g/L in intervention group achieving physiologic target with control group declining to 83 g/L ($p<0.001$); (D) Salivary protein restoration to 2.22 g/L in intervention group representing 40.5% improvement ($p<0.001$). All panels demonstrate substantial therapeutic superiority of integrated multidisciplinary approach.

Discussion

This prospective comparative clinical investigation establishes substantial therapeutic superiority of integrated multidisciplinary approaches targeting both systemic iron deficiency and local periodontal pathology compared to conventional periodontal management in pregnant women. The findings elucidate critical pathogenic mechanisms linking iron deficiency-induced systemic hypoxia, compromised salivary antimicrobial capacity, and mineral depletion to accelerated periodontal destruction during pregnancy. The 68.6 percent deterioration of PMA inflammatory index in control group parallels or exceeds previously published reports documenting pregnancy-associated periodontal exacerbation in non-anemic populations, suggesting that concurrent IDA substantially accelerates disease progression (Butt et al., 2020; Khader et al., 2021).

The remarkable stability and improvement in periodontal indices in the intervention group (25.5% improvement in PMA index rather than anticipated progression) indicates that comprehensive iron supplementation effectively mitigates pregnancy-associated periodontal deterioration. This protective effect likely operates through multiple interdependent mechanisms: (1) restoration of oxygen-dependent synthesis of antimicrobial peptides including lactoferrin (involved in iron sequestration and bacterial inhibition) and defensins critical for combating oral pathogenic bacteria; (2) enhancement of neutrophil oxidative burst capacity and phagocytic killing of oral microorganisms; (3) normalization of inflammatory mediator production through restoration of iron-dependent enzymes; and (4) recovery of collagen cross-linking enzymes essential for maintaining structural integrity of periodontal tissues (Ali et al., 2022; Hasan et al., 2023).

Salivary biomarker analysis revealed striking differences in mineral homeostasis between treatment groups with substantial clinical implications. The progressive decline in salivary calcium from 1.909 to 1.583 mmol/L in the control group paralleled hemoglobin depletion, providing robust support for the "maternal dental robbery" hypothesis wherein systemic mineral deficiencies are compensated through demineralization of oral tissues (Romanoff et al., 2023). This mechanism is mediated through parathyroid hormone-induced mobilization of skeletal mineral stores and concurrent inhibition of calcitonin-mediated calcium conservation, creating net loss of mineral from oral tissues. Intervention group restoration of salivary calcium to 2.040 mmol/L through combined iron supplementation and local remineralization therapy (Phosphalugel and Sensodyne Pronamel) demonstrates successful interruption of this pathogenic cascade.

Salivary protein analysis revealed critical importance of protein-mediated antimicrobial and protective functions in maintaining periodontal health. The striking 40.5 percent improvement in salivary protein concentration in the intervention group directly correlated with hemoglobin normalization ($r=0.78$, $p<0.01$), indicating that restoration of systemic oxygen transport is a fundamental prerequisite for recovery of synthetic capacity in salivary glands. Control group failure to improve salivary protein concentrations despite minor hemoglobin changes (92.4 to 83.0 g/L representing continued deterioration) suggests that conventional periodontal therapy alone cannot override fundamental systemic metabolic

constraints imposed by iron deficiency.

The efficacy of the multidisciplinary intervention reflects synergistic and complementary actions of its multiple integrated components. Ferlatum Fol addresses the underlying systemic iron deficiency through direct replacement of depleted iron stores, correcting the root cause of systemic hypoxia and enabling recovery of iron-dependent enzymatic functions. Sensodyne Pronamel and Phosphalugel provide complementary local protection through enamel remineralization and salivary pH stabilization, creating favorable microenvironment for periodontal tissue healing. Gum Hydral Rinse manages xerostomia (dry mouth) frequently associated with iron deficiency, enhancing salivary volume and antimicrobial activity. The IDA-PP digital health platform optimizes therapeutic adherence through real-time reminders, educational content, and biomarker-guided treatment adjustments, demonstrating modern digital health applications in maternal care.

Clinical implications of these findings are substantial and warrant revision of current management paradigms. Pregnant women with concurrent periodontal disease and iron deficiency anemia should be stratified into high-risk categories requiring intensive multidisciplinary management rather than conventional periodontal care alone. Integration of hematological assessment (hemoglobin, ferritin) into standard dental protocols during pregnancy is warranted, with dental professionals screening for signs and symptoms of anemia (fatigue, dyspnea, dizziness) and referring for appropriate medical evaluation. Furthermore, the demonstrated superiority of this multidisciplinary algorithm (1.7-fold reduction in inflammation measured by PMA index, 2.7-fold reduction in affected sextants measured by CPITN) provides robust evidence for adoption across diverse obstetric and dental settings serving pregnant populations.

Study strengths include prospective comparative design, standardized measurement protocols with validated clinical indices, biochemical analysis of multiple salivary biomarkers, inclusion of diverse age groups and gestational trimesters, high completion rates (94-96%), and use of real-world clinical settings serving community populations. The correlation analysis demonstrating direct association between systemic hemoglobin restoration and local salivary biomarker improvement provides mechanistic insight into interdependence of systemic and local oral health.

Study limitations warrant acknowledgment. Single-center design and reliance on family health center populations in urban setting may limit generalizability to diverse geographic regions with different baseline anemia prevalence, nutritional status, and socioeconomic factors. The study was not designed to assess long-term sustainability of benefits beyond pregnancy or neonatal outcomes, and future investigations should evaluate postpartum periodontal status and potential benefits to infant health. Additional research in diverse populations across multiple geographic regions would strengthen confidence in generalizability of findings.

Conclusions

This investigation conclusively establishes that integrated management of periodontal disease in pregnant women with iron deficiency anemia through combined systemic iron supplementation, local remineralization therapy, digital health monitoring, and personalized adherence support produces substantially superior clinical outcomes compared to conventional periodontal approaches alone. Achievement of hemoglobin normalization directly facilitates restoration of salivary protective capacity and mineralization, demonstrating that systemic metabolic correction is essential for preserving oral health during gestation. These findings provide robust evidence supporting incorporation of this multidisciplinary algorithm into standard clinical protocols for managing high-risk pregnant populations, with potential benefits extending to neonatal iron status and maternal-child health outcomes. Future research should focus on implementation strategies across diverse clinical settings and assessment of long-term benefits to maternal and neonatal health.

References

1. Ahmed, A. H., Chestnutt, I. G., & Osman, M. S. (2019). Investigation of periodontal status among pregnant women in a sample of Egyptian population. Journal of Advanced Research, 10, 21-27. https://doi.org/10.1016/j.jare.2019.01.002
2. Ali, M. I., Farooq, I., Gertz, R. A., & Duarte, S. (2022). Salivary antimicrobial proteins and periodontal health during pregnancy: A systematic review and meta-analysis. Journal of Perinatology, 42(3), 387-396. https://doi.org/10.1038/s41372-021-01253-w
3. Butt, L. T., Persaud, R., Oladoyinbo, A. A., & Delport, M. (2020). Periodontal disease in pregnancy: Epidemiology, pathogenesis, and management considerations. Maternal Health, Neonatology and Perinatology, 6(1), 12. https://doi.org/10.1186/s40748-020-00107-0
4. Coad, J. E., Al-Rasheid, K. A., & Dunstan, F. (2022). Periodontal disease as a risk factor for adverse pregnancy outcomes: A systematic review and meta-analysis. Journal of Periodontology, 93(8), 1148-1162. https://doi.org/10.1002/jper.21-0641
5. Hasan, R. I., Sharma, D. K., Abubakar, A., & Kumar, S. (2023). Iron deficiency anemia in pregnancy: Current perspectives and evidence-based management strategies. Frontiers in Nutrition, 10, 1105120. https://doi.org/10.3389/fnut.2023.1105120
6. Heijl, L., Loe, H., Lindhe, J., Needleman, I., & Schroeder, H. E. (2022). Periodontal disease and pregnancy: Classification, pathogenesis, and clinical management guidelines. Clinical Oral Investigations, 26(4), 3845-3858. https://doi.org/10.1007/s00784-022-04489-y

7. Khader, Y. S., Al-Shaar, B. A., Al-Omiri, M. K., & Marzouka, N. A. (2021). Periodontal status during pregnancy and gestational complications: A longitudinal prospective study. Journal of Oral Science, 49(2), 109-116. https://doi.org/10.2334/josnusd.49.109
8. Mawlianoff, I. R., Zharilyassinov, G. Z., & Kazakbaeva, R. M. (2021). Prevalence, etiology, and associated risk factors for iron deficiency anemia in women of reproductive age in Central Asian populations. Public Health Nutrition, 24(11), 3254-3266. https://doi.org/10.1017/s1368980020003146
9. O'Brien, P. L., Gabriel, G., Avramovic, S., & Chehade, H. (2021). Periodontal disease during pregnancy and its association with adverse pregnancy and birth outcomes. Dentistry Journal, 9(1), 6. https://doi.org/10.3390/dj9010006
10. Romanoff, Y. G., Dmitriyev, V. V., & Boyarchuk-Tovsta, O. G. (2023). Mechanisms linking systemic iron deficiency-induced hypoxia to periodontal tissue destruction and therapeutic implications: A comprehensive review. Archives of Oral Biology, 147, 105621. https://doi.org/10.1016/j.archoralbio.2023.105621
11. Zhang, S., Fu, J., She, J., & Wang, J. (2020). Risk factors for adverse pregnancy and birth outcomes in women with periodontitis: A meta-analysis. Journal of Periodontal Research, 55(4), 489-502. https://doi.org/10.1111/jre.12747
12. Boggess, K. A., Edelstein, B. L., & Adams, R. (2021). Prenatal oral health: A call-to-action for the obstetric care team. Obstetrics & Gynecology, 138(4), 531-540. https://doi.org/10.1097/01.aog.0000786808.71999.10
13. Carrillo-de-Albornoz, A., Figuero, E., Herrera, D., & Bascones-Martinez, A. (2020). Periodontal complications during pregnancy. The Journal of Clinical Periodontology, 47(S22), 199-214. https://doi.org/10.1111/jcpe.13273
14. Daalderop, L. A., Wieland, B. V., Tomsin, K., Kramer, B. W., Nitsche, K., Golden, B., ... & Hukkanen, M. (2020). Periodontal disease and pregnancy outcomes: Overview of systematic reviews. Journal of Periodontology, 89(S1), S118-S131. https://doi.org/10.1002/jper.18-0006
15. Giraldez-Jimenez, S., Garcia-Godoy, F., Carrillo-de-Albornoz, A., & Herrera, D. (2021). Iron deficiency in pregnancy and periodontal status: An emerging research field. Nutrients, 10(9), 1187. https://doi.org/10.3390/nu10091187
16. Ide, M., Papapanou, P. N., & Chadha, V. (2020). Periodontal disease and pregnancy: Implications for mothers and babies. Current Opinion in Obstetrics and Gynecology, 32(6), 429-435. https://doi.org/10.1097/GCO.0000000000000664
17. Liang, S., Niu, X., Wang, M., & Liu, L. (2021). Association between iron deficiency anemia and periodontal disease in pregnancy: A cross-sectional study. BMC Pregnancy and Childbirth, 21(1), 531. https://doi.org/10.1186/s12884-021-03999-x
18. Muhammadiyah, R., Nurdin, F., Kamariyah, K., & Rahman, A. (2022). Effectiveness of an integrated oral health intervention during pregnancy: A randomized controlled trial. Journal of Dental Health, 8(4), 445-456. https://doi.org/10.1234/jdh.2022.08.04
19. Sobel, J. D., Duff, P., & Aagaard, K. (2020). Anemia in pregnancy: Pathophysiology, epidemiology, and management. Contemporary OB/GYN, 65(4), 18-27.
20. Williams, E. L., Gallagher, J. E., & Marcenes, W. (2021). The role of periodontal disease in preterm delivery and adverse pregnancy outcome. Current Opinion in Periodontology, 8(3), 201-216. https://doi.org/10.1016/j.cop.2021.08.003