



(RESEARCH ARTICLE)



THE RELATIONSHIP BETWEEN HIGH-DENSITY LIPOPROTEIN LEVELS AND EARLY WOUND HEALING AFTER MANDIBULAR THIRD MOLAR ODONTECTOMY IN SMOKERS

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ABSTRACT

Background: Smoking is associated with impaired postoperative healing and alterations in lipid metabolism, including reduced high-density lipoprotein (HDL) levels. HDL has anti-inflammatory, antioxidant, endothelial, and tissue-repair functions, but its relationship with early intraoral wound healing after mandibular third molar odontectomy remains insufficiently explored.

Objective: To determine the relationship between HDL levels and wound healing after mandibular third molar odontectomy and to compare HDL levels and wound-healing scores between smokers and non-smokers.

Methods: This analytical observational study used a cross-sectional approach and purposive sampling. Ten male patients aged 19–36 years undergoing mandibular third molar odontectomy at the Dental Hospital of Universitas Airlangga were included, comprising five smokers and five non-smokers. Serum HDL was measured using a TMS Premium 24i analyzer. Early wound healing was assessed at postoperative day 2 (H+2) and day 8 (H+8) using the Early Wound Healing Score (EHS). Between-group comparisons and Pearson correlation analyses were performed using a significance level of $p < 0.05$.

Results: Mean HDL was 37.6 ± 3.05 mg/dL in smokers and 45.4 ± 2.61 mg/dL in non-smokers ($p = 0.002$). Mean wound-healing scores were lower in smokers at H+2 (4.8 ± 0.84 vs 7.8 ± 0.84 ; $p < 0.001$), while the difference at H+8 was not statistically significant (6.2 ± 1.92 vs 8.0 ± 2.00 ; $p = 0.185$). HDL was positively correlated with wound-healing score at H+2 ($r = 0.686$; $p = 0.029$), but not at H+8 ($r = 0.561$; $p = 0.091$).

Conclusion: Lower HDL levels and poorer early wound-healing scores were observed in smokers. HDL showed a significant positive association with wound-healing quality at H+2, although the small sample and limited inter-rater reliability warrant cautious interpretation.

Keywords: High-Density Lipoprotein; Smoking; Odontectomy; Mandibular Third Molar; Wound Healing; Early Wound Healing Score

1 INTRODUCTION

Mandibular third molar odontectomy is a common oral surgical procedure performed for impacted teeth. Although generally predictable, postoperative complications and disturbances in wound healing may occur. Reported complications after third molar surgery include pain, swelling, trismus, bleeding, paresthesia, and alveolar osteitis, with smoking recognized as one of the patient-related factors associated with postoperative complications^{1,2}. In smokers, exposure to tobacco constituents may interfere with local vascularity, inflammation, oxygen delivery, and tissue repair, thereby creating a biologically less favorable environment for healing^{3,4}.

Nicotine is a major contributor to these effects. Tobacco exposure promotes sympathetic activation and vasoconstriction, while other smoke constituents can contribute to oxidative stress and altered inflammatory responses^{3,4}. Smoking is also associated with changes in lipid metabolism. HDL is a heterogeneous lipoprotein with functions extending beyond reverse cholesterol transport, including modulation of inflammation, oxidative stress, endothelial function, and immune responses⁵. Changes in HDL concentration and function may therefore be relevant to tissue repair.

Clinical studies have reported lower HDL concentrations or altered lipoprotein profiles among smokers. A study summarized in the thesis literature showed a significant difference in HDL between conventional smokers and non-smokers, while a more recent analysis of smokers and non-smokers also supports an association between smoking and lipid abnormalities^{6,7}. Smoking-related alterations in apolipoproteins and HDL function may further compromise the protective properties of HDL⁷.

Wound healing is a coordinated process involving hemostasis, inflammation, proliferation, angiogenesis, re-epithelialization, and remodeling. Oral mucosa has distinctive healing characteristics and can heal efficiently because of its vascularity and local biological environment⁸. Nevertheless, systemic metabolic disturbances and smoking may alter the quality of this response. HDL has been linked to wound healing in systemic conditions; in patients with diabetic foot ulcers, lower HDL cholesterol was associated with poorer wound-healing outcomes⁹. HDL-related antioxidant and endothelial effects may be biologically relevant because oxidative stress and impaired perfusion can interfere with cellular migration, angiogenesis, and re-epithelialization.

The present study was designed to examine this relationship in the specific clinical setting of mandibular third molar odontectomy. The study compared serum HDL and early wound-healing scores between smokers and non-smokers and examined whether HDL concentration was associated with the quality of healing at postoperative day 2 and day 8. The objective was to provide preliminary clinical evidence regarding HDL as a potential biological factor associated with early postoperative wound healing in smokers.

2 MATERIALS AND METHODS

2.1 Study design and setting

This analytical observational study used a cross-sectional approach. Data collection was performed at the Dental Hospital of Universitas Airlangga (RSGM-P Universitas Airlangga), Surabaya, from September to November 2025. The study protocol involved assessment of smoking status, serum HDL concentration, and postoperative wound healing after mandibular third molar odontectomy.

2.2 Participants and sampling

Participants were recruited using non-probability purposive sampling. Of 52 patients initially assessed through the screening questionnaire, 10 participants met the study criteria and completed the study: five active smokers and five non-smokers. All participants were male and aged 19–36 years. The controlled clinical characteristics included mandibular third molar impaction classified as class II, absence of major systemic disease, BMI below 30 kg/m², local anesthesia, triangular flap technique, standardized postoperative antibiotic and analgesic therapy, and surgery performed by oral and maxillofacial surgery residents who had completed at least 50 odontectomy procedures.

Screening criteria included patients scheduled for mandibular third molar odontectomy, no blood transfusion within the preceding three months, adequate sleep (7–8 hours/day), no cancer, hormonal disorder, systemic disease, immune disorder, alcohol consumption, or relevant medication use. Inclusion criteria were active smokers or non-smokers aged 18–39 years. Exclusion criteria included unwillingness or inability to participate, pregnancy or hormonal disorders, exclusive e-cigarette use, systemic diseases such as cardiovascular disease, diabetes, renal or blood disorders, lipid-lowering medication, immune disorders, alcohol consumption, and obesity (BMI ≥30 kg/m²).

2.3 HDL measurement

Approximately 5 mL of venous blood was collected from the median cubital vein. Serum was obtained after centrifugation and stored at -80°C until analysis. HDL concentration was analyzed at the Research Laboratory Installation, Universitas Airlangga, using a TMS Premium 24i analyzer. The laboratory procedure used HDL R1 and R2 reagents according to the laboratory workflow. Serum samples were centrifuged to obtain serum, aliquoted into microtubes, stored at -80°C , and subsequently thawed before HDL analysis¹⁰.

2.4 Odontectomy and wound assessment

All participants underwent mandibular third molar odontectomy under local anesthesia. Postoperative wound assessment was performed at H+2 and H+8. Intraoral clinical photographs were obtained using an iPhone 16 with a 12-megapixel camera. The recorded photographic settings were ISO 32, shutter speed 1/15 s, exposure 0 EV, and approximately 62-mm zoom. Wound healing was evaluated using the Early Wound Healing Score (EHS), comprising clinical signs of re-epithelialization, hemostasis, and inflammation. Re-epithelialization was scored 0, 3, or 6; hemostasis 0–2; and inflammation 0–2, giving a total EHS range of 0–10. Three oral and maxillofacial surgery clinicians assessed the clinical images. Because inter-rater agreement was limited, the median score from the three evaluators was used as the final score for each participant.

2.5 Statistical analysis

Data were analyzed using SPSS. Shapiro–Wilk testing was used to assess normality and Levene’s test to assess homogeneity of variance. Independent-samples t-tests were used for normally distributed homogeneous variables, while the Mann–Whitney test was used where the normality assumption was not met. Pearson correlation was used to assess the relationship between HDL concentration and wound-healing score, consistent with the original analysis. Because EHS is an ordinal score, Spearman rank correlation should be considered as a sensitivity analysis in future analysis of the raw patient-level data. Statistical significance was set at $p < 0.05$. Effect sizes for the difference in HDL between groups were also calculated.

2.6 Ethical considerations

Ethical approval was obtained from the Dental Hospital Airlangga University Health Research Ethical Clearance Commission under certificate number 44/UN3.9.3/Etik/PT/2025, issued in Surabaya on 9 October 2025. Written informed consent was obtained from all participants before enrollment and blood collection.

3 RESULTS AND DISCUSSION

3.1 Participant characteristics

Ten participants completed the study, with five smokers and five non-smokers. The mean age was 25.2 ± 5.21 years in smokers and 23.8 ± 6.99 years in non-smokers; the between-group difference was not significant (Mann–Whitney $p = 0.462$). Mean BMI was 26.06 ± 3.49 kg/m^2 in smokers and 22.44 ± 4.15 kg/m^2 in non-smokers, with no significant difference (independent t-test $p = 0.174$). Mean Pederson scores were identical at 5.6 in both groups, indicating comparable surgical difficulty based on the study’s controlled sample characteristics.

Table 1: Participant characteristics and HDL concentration.

Variable	Smokers (n=5)	Non-smokers (n=5)	P value
Age, years	25.2 ± 5.21	23.8 ± 6.99	0.462
BMI, kg/m^2	26.06 ± 3.49	22.44 ± 4.15	0.174
Pederson score	5.6 ± 1.14	5.6 ± 1.52	>0.05
HDL, mg/dL	37.6 ± 3.05	45.4 ± 2.61	0.002

Among smokers, three participants (60%) were categorized as light smokers (1–10 cigarettes/day), two (40%) as moderate smokers (11–20 cigarettes/day), and none as heavy smokers (>20 cigarettes/day).

3.2 HDL concentration

Mean HDL concentration was significantly lower in smokers (37.6 ± 3.05 mg/dL) than in non-smokers (45.4 ± 2.61 mg/dL), with $p = 0.002$. Both groups showed normal HDL distributions and homogeneous variances. The estimated effect

was large, with Cohen's $d=2.749$, Hedges' correction= 2.482 , and Glass's delta= 2.558 . Given the sample size of only five participants per group, these estimates should be interpreted as preliminary rather than definitive.

The lower HDL concentration observed in smokers is biologically plausible. Smoking has been associated with dyslipidemia and altered apolipoprotein concentrations, and tobacco exposure may affect both HDL concentration and function^{6,7}. HDL participates in reverse cholesterol transport and has anti-inflammatory and antioxidant properties. HDL-related protection of endothelial function and modulation of inflammatory signaling provide a possible link between lipid status and tissue repair⁵. In the present study, the lower HDL concentration in smokers therefore provides a potential biological context for the poorer early wound scores observed after surgery.

3.3 Early wound-healing scores

Table 2: Early wound-healing scores at H+2 and H+8.

Outcome	Smokers	Non-smokers	P value
EHS H+2, mean $\pm$ SD	4.8 $\pm$ 0.84	7.8 $\pm$ 0.84	<0.001
EHS H+8, mean $\pm$ SD	6.2 $\pm$ 1.92	8.0 $\pm$ 2.00	0.185

At H+2, the mean wound-healing score was 4.8 $\pm$ 0.84 in smokers and 7.8 $\pm$ 0.84 in non-smokers, with a statistically significant difference ($p<0.001$). At H+8, the mean score remained lower in smokers (6.2 $\pm$ 1.92) than in non-smokers (8.0 $\pm$ 2.00), but the difference was not statistically significant ($p=0.185$). Thus, the clearest between-group difference was observed during the early postoperative period.

The H+2 finding is consistent with the known effects of smoking on the early inflammatory and vascular stages of healing. Smoking can reduce tissue perfusion through vasoconstriction and contribute to oxidative and inflammatory disturbances^{3,4}. These effects may be particularly visible shortly after surgery, when hemostasis, inflammation, and early re-epithelialization dominate the wound response. The oral mucosa generally heals efficiently, but systemic and local factors can alter the quality of this process⁸.

The absence of a statistically significant difference at H+8 should not be interpreted as evidence that smoking has no effect on later healing. The direction of the difference remained the same, with a 1.8-point higher mean score in non-smokers. Several factors may explain the reduced statistical separation at H+8, including the very small sample, biological convergence during the proliferative phase, and low inter-rater reliability. In addition, the EHS was originally designed to capture early wound characteristics, making later assessments more vulnerable to subtle visual differences.

3.4 Relationship between HDL and wound healing

Table 3: Correlation between HDL concentration and wound-healing score.

Correlation	Pearson r	P value	Interpretation
HDL vs EHS H+2	0.686	0.029	Positive, strong; statistically significant
HDL vs EHS H+8	0.561	0.091	Positive, moderate; not statistically significant

Pearson analysis demonstrated a positive correlation between HDL and wound-healing score at H+2 ($r=0.686$; $p=0.029$). Thus, participants with higher HDL concentrations tended to have better early wound-healing scores. At H+8, the correlation remained positive but was weaker and did not reach statistical significance ($r=0.561$; $p=0.091$). Because the correlation was calculated from all 10 participants combined, the observed association may partly reflect the between-group differences in both HDL concentration and wound-healing scores rather than a within-group relationship.

The significant H+2 association supports the hypothesis that HDL may be relevant to early wound repair. HDL is involved in anti-inflammatory and antioxidant processes and can influence endothelial function and nitric oxide bioavailability⁵. These functions are relevant to perfusion and tissue repair after surgical injury. Experimental and clinical evidence cited in the thesis also links lower HDL with poorer wound healing in systemic wounds, particularly diabetic foot ulcers⁹. The present study extends this observation to an intraoral postoperative setting, although the cross-sectional observational design cannot establish a causal effect.

The non-significant H+8 correlation may reflect the changing biological contribution of HDL during healing, increased inter-individual variation, or measurement limitations. It may also be affected by the low reliability of wound scoring. At H+2, the intraclass correlation coefficient was 0.295 for single measures and 0.556 for average measures ($p=0.068$). At H+8, the corresponding values were 0.019 and 0.055 ($p=0.436$). The use of median scores reduced the influence of individual extreme ratings but cannot completely eliminate measurement error.

The findings should therefore be interpreted as preliminary evidence of association rather than proof that low HDL causes delayed wound healing. The correlation analysis was based on only 10 participants and combined the smoker and non-smoker groups; within-group correlations were not analyzed because of the very small group sizes. In addition, EHS is an ordinal clinical score, and the use of Pearson correlation may not fully reflect its distributional characteristics. Other determinants of HDL and wound repair, including diet, physical activity, body composition, genetics, surgical trauma, local perfusion, oral hygiene, and smoking intensity, may have contributed to the observed relationship. The present study controlled several clinical factors, including BMI threshold, systemic disease, surgical technique, operator experience, and postoperative treatment, but did not fully quantify dietary or physical-activity exposures.

3.5 Clinical and research implications

From a clinical perspective, the findings suggest that lipid status may be relevant when considering the biological context of postoperative healing in smokers. However, the current sample is too small to support routine HDL screening as a clinical decision rule. The main value of the present study is hypothesis generation: it identifies an association that can be tested in larger prospective cohorts with adequate adjustment for confounding variables.

Future studies should recruit substantially larger samples and use standardized photographic conditions and evaluator calibration to improve wound-score reliability. They should also assess smoking intensity and duration quantitatively, include comprehensive lipid profiles, and measure dietary intake and physical activity. Spearman rank correlation or other methods appropriate for ordinal wound scores should be considered alongside Pearson correlation. Analyses within each smoking group would also help determine whether the HDL–healing relationship persists independently of smoking status. Including non-smokers with low HDL would be particularly useful for separating the effect of HDL concentration from the effect of smoking itself. Longer follow-up and direct clinical assessment of complications such as infection, wound dehiscence, and alveolar osteitis would further strengthen the clinical relevance of the findings.

4 CONCLUSION

In this preliminary study of 10 patients undergoing mandibular third molar odontectomy, smokers had significantly lower mean HDL concentrations than non-smokers and significantly poorer early wound-healing scores at H+2. HDL concentration showed a significant positive correlation with wound-healing score at H+2, whereas the positive correlation at H+8 was not statistically significant. The findings support an association between HDL status and early postoperative wound-healing quality, particularly during the early phase of healing. Because of the very small sample and limited inter-rater reliability, the results should be considered exploratory and require confirmation in larger, well-controlled studies.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The author declares no financial or non-financial conflict of interest related to this study.

Statement of ethical approval

The study was approved by the Dental Hospital Airlangga University Health Research Ethical Clearance Commission, certificate No. 44/UN3.9.3/Etik/PT/2025, dated 9 October 2025.

Statement of informed consent

Written informed consent was obtained from all participants before participation and blood collection.

Consent for publication

Not applicable; no individually identifiable participant information is presented in this manuscript.

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