IRAQI Academic Scientific Journals NINEVAH UNIVERSITY JOURNAL OF MEDICAL SCIENCES Vol. 1, Issue 2, December 2025

NINEVAH UNIVERSITY NUJMS Journal of Medical Sciences

ISSN 3106-5430 (print)

ARTICLE

Cigarette Smoking and Early Biochemical Indicators of Bone and Metabolic Health in Iraqi Adult Males

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Article information:

Received	2 Jun, 2025
Received in revised form	14 September, 2025
Accepted	15 September, 2025
Final Proofreading	24 December, 2025
Published	31 December, 2025

DOI Online:

http://doi.org/10.64554/nujms.2025.1.2.7

Keywords:

Alkaline phosphatase; Body mass index; Bone metabolism; Cigarette smoking; Vitamin D; Waist circumference.

ABSTRACT

Background : Cigarette smoking has emerged as a significant extrinsic factor influencing skeletal and metabolic homeostasis, primarily through its modulation of vitamin D metabolism, enzymatic activity associated with bone turnover, and alterations in body composition indices. These disturbances may have cumulative implications for bone integrity and systemic health.

Objective: This study aimed to elucidate the potential effects of cigarette smoking on serum 25-hydroxyvitamin D levels, alkaline phosphatase activity, body mass index, and waist circumference among apparently healthy adult Iraqi males.

Methods: A Cross sectional comparative study was conducted between September 2024 and March 2025, involving 240 adult males (n = 120 smokers; n = 120 non-smokers), stratified by age into two subgroups (20–34 and 35–50 years). Anthropometric and biochemical parameters were assessed using standardized procedures. Vitamin D and alkaline phosphatase were measured via Roche/Hitachi Cobas analyzers. Statistical analysis included t-tests, ANOVA, and Pearson's correlation coefficients; $p < 0.05$ was considered significant.

Results: Although mean serum vitamin D levels did not significantly differ between groups, a substantially higher prevalence of vitamin D deficiency was observed among smokers (75.83%) compared to non-smokers (64.17%). In smokers, alkaline phosphatase levels were positively correlated with both age and smoking duration ($p = 0.011$ and $p = 0.045$, respectively). Among non-smokers, advancing age was significantly associated with increased body mass index and waist circumference ($p = 0.043$), as well as a notable decline in vitamin D levels ($p = 0.017$). A robust inverse correlation was detected between WC and vitamin D among smokers ($r = –0.595$, $p < 0.001$).

Conclusion: The findings suggest that chronic tobacco exposure is associated with a higher prevalence of vitamin D deficiency. In contrast, non-smokers exhibited age-dependent metabolic alterations. These data underscore the need for vitamin D level surveillance and metabolic risk screening in smokers.

Introduction

Cigarette smoking is widely recognized as a critical behavioral determinant contributing to the etiology of multiple chronic conditions, including cardiovascular dysfunction, pulmonary pathologies, and carcinogenesis. Beyond these systemic effects, accumulating evidence has illuminated its potential role in disrupting skeletal homeostasis and altering key metabolic parameters, most notably through interference with vitamin D metabolism and hormonal regulation of bone remodeling pathways [1][2].

Vitamin D serves as a cornerstone in maintaining calcium–phosphate equilibrium and facilitating normal bone mineralization. Its active metabolite, 1,25-dihydroxyvitamin D, arises

via hepatic and renal hydroxylation processes that are tightly modulated by parathyroid hormone levels. Disruption of this axis—whether through impaired absorption, metabolic inactivation, or sequestration in adipose tissue—has been increasingly linked to tobacco exposure, independent of lifestyle factors such as sunlight exposure or dietary intake [3][4].

In parallel, alkaline phosphatase (ALP), a well-characterized enzymatic biomarker of osteoblastic activity, may be modulated by chronic smoking-induced oxidative stress and systemic inflammation, thereby reflecting compensatory bone turnover[5]. Moreover, smoking exerts complex effects on body composition: while nicotine is known to suppress appetite and reduce body weight, paradoxical increases in central adiposity have been documented, often manifesting as elevated waist circumference [6].

Notably, visceral adiposity has been inversely correlated with serum vitamin D concentrations, likely due to volumetric dilution and hormonal inactivation, further complicating the interpretation of vitamin D status in smokers [7].

Despite the growing body of literature on these associations, region-specific data—particularly from Middle Eastern populations—remain scarce. The present study was therefore designed to critically evaluate the impact of cigarette smoking on serum vitamin D levels, ALP activity, BMI, and waist circumference among healthy adult males in Iraq, with particular emphasis on age stratification and smoking intensity.

Methods

Materials and Methods

1. Study Design and Setting

A cross-sectional comparative study–conducted over a six-month period, from September 2024 to March 2025, at The Consultative Fragility Unit, Rheumatology Division, Department of Internal Medicine, Ibn Sina Hospital. The study aimed to evaluate the impact of cigarette smoking on bone-related biochemical and anthropometric indices among apparently healthy adult males.

Ethical Approval: This study was reviewed and approved by the Ethics Committee of the Ministry of Health and Environment, Iraq (Approval No. 2021/02, Directorate of Research Approval). All experimental procedures were conducted in accordance with the ethical guidelines and regulations of the Ministry of Health and Environment.

2. Study Population and Grouping

Participants were recruited using simple random sampling techniques. The sample size of 240 participants (120 smokers and 120 non-smokers) was calculated based on a statistical power analysis using an expected medium effect size (Cohen's d = 0.5), a significance level of 0.05, and a statistical power of 0.80. This calculation indicated that at least 102 subjects per group were required; therefore, the sample size was increased to 120 per group to compensate for potential dropouts and to strengthen the validity of subgroup analyses.

The sample aged between 20 and 50 years, equally divided into two groups: 120 smokers and 120 non-smokers. The case group (smokers) was recruited from Ibn-Sina Hospital and from staff and students at the Mosul Medical Technical Institute. The smoker group was further stratified based on smoking intensity and duration, using the smoking index, calculated as follows:

Smoking Index = Number of cigarettes per day × Number of years of smoking

With classification as:

Mild smoking: ≤ 200

Moderate smoking: 201–399

Severe smoking: ≥ 400

ISSN 3106-5430 (print)
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3. Inclusion and Exclusion Criteria

Written informed consent was obtained from all participants prior to inclusion in the study, in accordance with the Declaration of Helsinki.

Inclusion criteria included healthy males aged 20–50 years who are currently cigarette smokers.

Exclusion criteria included:

History of bone metabolic disorders (e.g., osteoporosis, osteomalacia)

Current use of calcium or vitamin D supplements

Presence of endocrine disorders or renal insufficiency

Alcohol consumption or illicit drug use

4. Anthropometric Measurements

Body weight was measured using a calibrated digital scale to the nearest 0.1 kg. Height was recorded to the nearest 0.5 cm using a stadiometer.

Body Mass Index (BMI) was calculated as:

$BMI = \text{Weight (kg)} / [\text{Height (m)}]^2$

BMI classification followed WHO criteria: [7]

Underweight: < 18.5

Normal: 18.5–24.9

Overweight: 25–29.9

Obese Class I: 30–34.9

Obese Class II: 35–39.9

Obese Class III: ≥ 40

Waist circumference (WC) was measured using a non-elastic tape at the midpoint between the lower rib margin and the iliac crest during end-expiration [8].

5. Biochemical Assays

Venous blood samples were collected after an overnight fast. Serum was separated and analyzed using the Roche/Hitachi Cobas automated system for the following parameters:

25-hydroxyvitamin D (25(OH)D): measured in ng/mL and categorized as follows: [9].

Deficiency: < 20 ng/mL

Insufficiency: 21–29 ng/mL

Sufficiency: ≥ 30 ng/mL

Toxicity: > 150 ng/mL

Alkaline Phosphatase (ALP): measured in U/L; normal reference range for adult males: 40–129 U/L [10].

6. Instruments and Analytical Kits

The equipment and tools used in the study included the 25(OH) Vitamin D Assay Kit and the Alkaline Phosphatase Assay Kit, both manufactured by Roche Diagnostics, Germany. Biochemical analyses were performed using the Cobas c501 Autoanalyzer (Roche/Hitachi, Switzerland/Japan [11]. Anthropometric measurements were obtained using standardized tools such as a non-elastic measuring tape and a calibrated scale.

All tests were conducted following standard laboratory protocols and manufacturer guidelines.

7. Statistical Analysis

Data were analyzed using IBM SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as means ± standard deviations (SD) for continuous variables. Inferential analyses included [12]:

Independent samples t-test for between-group comparisons

One-way analysis of variance (ANOVA) to compare subgroups

Pearson correlation coefficient for evaluating associations between continuous variables

A p-value < 0.05 was considered statistically significant in all analyses.

Result

Table 1 summarizes the age distribution of the study population, indicating that smokers and non-smokers were nearly equally represented across the two age categories, with a slightly higher proportion of younger individuals in the non-smoker group. In addition, the comparison of mean age between groups showed no statistically significant difference (34.17 ± 9.89 years in smokers vs. 32.94 ± 9.58 years in non-smokers; p = 0.331).

Table 1: Distribution of the age groups within subdivided study sample

Age (years)	Smokers (n = 120)	%	Non-smokers (n = 120)	%	p-value
20–34	61	50.8	68	56.7	
35–50	59	49.2	52	43.3	
Total	**120**	100.0	**120**	100.0	
Mean ± SD	34.17 ± 9.89	—	32.94 ± 9.58	—	0.331

The results in Tables 2A and 2B indicate that the mean waist circumference was significantly higher in non-smokers compared with smokers (p = 0.049), while no significant difference was observed in mean BMI between the two groups (p = 0.240). Age-stratified analysis further showed that older non-smokers (35–50 years) had significantly greater waist circumference (p = 0.043) and BMI compared to younger non-smokers, whereas no significant age-related differences in these parameters were detected among smokers. These findings suggest that the progression of central adiposity and BMI with advancing age is more evident in non-smokers than in smokers.

Table 2A. Anthropometric parameters by smoking status

Parameter	Smokers (n = 120) Mean ± SD	Non-smokers (n = 120) Mean ± SD	p-value
Waist circumference (cm)	95.25 ± 13.00	98.50 ± 12.50	0.049
BMI (kg/m²)	26.65 ± 5.28	27.48 ± 5.66	0.240

Table 2B. Anthropometric parameters stratified by age within smoking and non-smoking groups

Group	Parameter	Age 20–34 (Mean ± SD)	Age 35–50 (Mean ± SD)	p-value
Smokers (n = 120)	Age (years)	34.17 ± 9.89	32.94 ± 9.58	0.369
	Waist circumference (cm)	94.20 ± 11.83	96.34 ± 14.13	0.331
	BMI (kg/m²)	26.06 ± 6.04	27.27 ± 4.32	0.210
Non-smokers (n = 120)	Waist circumference (cm)	96.49 ± 13.15	101.13 ± 11.65	0.043*

indicate no statistically significant difference in mean vitamin D or ALP levels between smokers and non-smokers. However, within-group analysis shows that older non-smokers (35–50 years) had significantly lower vitamin D levels compared to younger non-smokers (p = 0.017), while smokers showed no age-related change. ALP levels did not differ significantly by age in either group, suggesting that age-related decline in vitamin D is more evident among non-smokers.

Table 3. Biochemical parameters stratified by age within smoking and non-smoking groups

Group	Parameter	Age 20–34 (Mean ± SD)	Age 35–50 (Mean ± SD)	p-value
Smokers (n = 120)	Vitamin D (ng/mL)	17.64 ± 5.85	17.14 ± 9.26	0.722
	ALP (U/L)	80.27 ± 12.58	83.23 ± 12.06	0.063
Non-smokers (n = 120)	Vitamin D (ng/mL)	20.62 ± 10.96	15.92 ± 9.87	0.017*
	ALP (U/L)	83.23 ± 12.06	—	—

The results in **Table 4** show no statistically significant differences in vitamin D, ALP, BMI, or waist circumference across the three smoking duration categories (< 5 years, 5–10 years, > 10 years). Although mean ALP and BMI values were slightly higher in the 5–10 year group, these differences did not reach statistical significance, indicating that the duration of smoking in this cohort was not associated with measurable changes in the assessed biochemical or anthropometric parameters.

Table 4: Study Variables by Smoking Duration

Variable	Duration	n	Mean ± SD	p-value
Vitamin D (ng/mL)	< 5 years	16	15.83 ± 4.05	0.644
	5–10 years	39	17.29 ± 5.89	
	> 10 years	65	17.84 ± 9.20	
ALP (U/L)	< 5 years	16	76.44 ± 10.59	0.361
	5–10 years	39	79.92 ± 13.47	
	> 10 years	65	81.42 ± 12.45	
BMI (kg/m²)	< 5 years	16	24.97 ± 4.18	0.264
	5–10 years	39	27.51 ± 6.83	
	> 10 years	65	26.55 ± 4.33	
WC (cm)	< 5 years	16	93.88 ± 12.70	0.888
	5–10 years	39	95.77 ± 10.40	
	> 10 years	65	95.28 ± 14.54	

Figure 3 illustrates the correlations of serum vitamin D and ALP with age, number of cigarettes smoked per day, and smoking duration among smokers. Vitamin D showed weak positive associations with age, cigarette consumption, and smoking duration, whereas ALP displayed slight negative correlations with age and cigarettes/day but a marginal positive trend with smoking duration. None of these associations reached strong statistical significance.

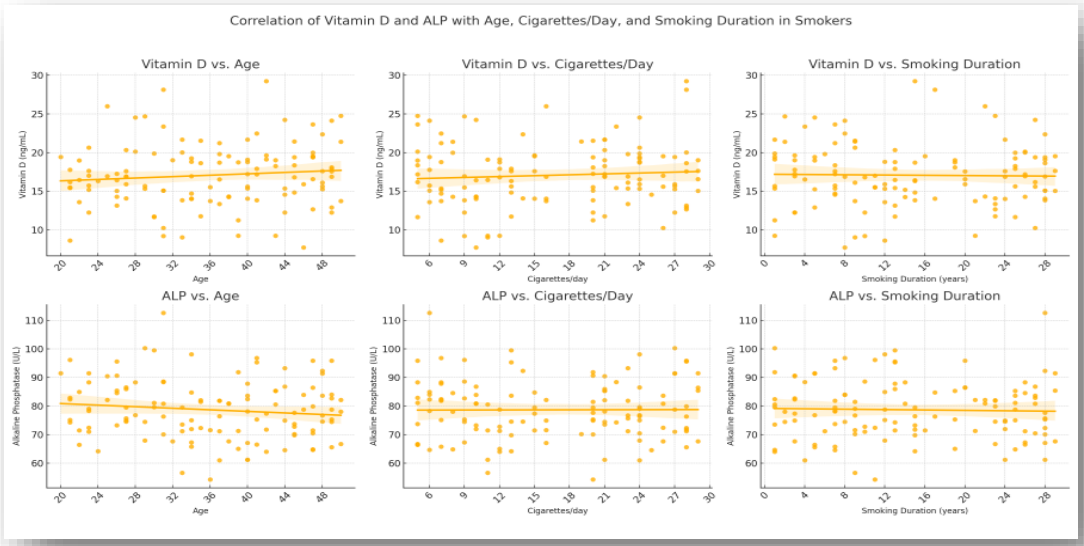

Figure 3 illustrates the correlations between serum 25(OH)D and ALP with age, daily cigarette consumption, and smoking duration among smokers (Panels A–F).

Discussion

The findings of the present study reveal a higher prevalence of vitamin D deficiency among smokers compared to their non-smoking counterparts (75.83% vs. 64.17%), despite the absence of a statistically significant difference in mean serum vitamin D concentrations. This discrepancy highlights that even small reductions in mean values can lead to significant shifts in distribution, resulting in a higher proportion of individuals falling into the deficient category. These results are congruent with prior global evidence, including a comprehensive meta-analysis [1][13], which concluded that cigarette smoking is a consistent and independent predictor of lower circulating 25(OH)D levels across various populations. The underlying mechanisms are multifactorial and may include impaired intestinal absorption, accelerated metabolic clearance of vitamin D due to hepatic enzyme induction, and decreased synthesis in the skin due to vascular changes associated with chronic nicotine exposure [1][4].

Although the within-group analysis revealed a significant age-related decline in vitamin D levels among non-smokers, the substantially higher prevalence of vitamin D deficiency in smokers compared with non-smokers underscores that smoking exerts an additional adverse effect beyond the natural influence of age. This suggests that both chronological aging and tobacco exposure act as independent yet overlapping determinants of vitamin D status.

Although ALP values remained within the normal reference range for both groups, smokers exhibited a modest but statistically significant positive correlation between ALP levels and both age ($r = 0.230$; $p = 0.011$) and smoking duration ($r = 0.184$; $p = 0.045$). These findings may be more consistent with age-related variations in ALP activity, rather than a direct stimulatory effect of smoking, suggesting that age exerts a stronger influence on bone turnover markers in this cohort. Similar observations were reported elevated ALP activity in long-term smokers, possibly linked to osteoblastic compensation for bone microdamage [6] [10] [14].

Notably, smoking intensity—as measured by the number of cigarettes smoked per day—did not exhibit statistically significant correlations with any of the biochemical markers analyzed, including vitamin D and ALP. This suggests that cumulative exposure duration may be a more critical determinant of physiological disruption than daily quantity alone. This notion is supported by [15][16] who emphasized the importance of long-term exposure metrics in evaluating tobacco-related metabolic alterations [14][17].

Taken together, these findings underscore the multifaceted interactions between smoking, vitamin D status, adiposity, and bone enzymatic activity. They highlight the importance of incorporating vitamin D screening and metabolic risk assessment in public health strategies targeting tobacco users. Furthermore, the data call for longitudinal investigations to elucidate the long-term skeletal and metabolic consequences of chronic smoking exposure in diverse populations.

Conclusion

The present study underscores the significant association between chronic cigarette smoking and biochemical indicators of skeletal health, particularly the elevated prevalence of vitamin D deficiency and age-related increases in serum alkaline phosphatase levels. Although the mean values for both vitamin D and ALP remained within physiological reference ranges, the identified correlations with smoking duration and age suggest a latent, cumulative impact on bone metabolism that may precede overt clinical manifestations.

Taken together, these findings reinforce existing evidence that tobacco use disrupts metabolic and skeletal homeostasis and call for the integration of vitamin D screening, lifestyle interventions, and risk stratification protocols within smoking cessation programs.

Future Perspectives

To build upon the current findings, future studies should adopt longitudinal cohort designs to delineate the temporal evolution of vitamin D depletion and bone turnover in relation to cumulative smoking exposure. The inclusion of additional biomarkers—such as parathyroid hormone (PTH), osteocalcin, and C-terminal telopeptide (CTX)—would offer a more comprehensive assessment of skeletal remodeling dynamics.

Moreover, expanding the study population to include females, postmenopausal individuals, and older adults would enhance generalizability and clarify gender- and age-specific vulnerabilities. Investigating the reversibility of these alterations through interventional trials—particularly vitamin D supplementation in smokers—may further elucidate the potential for metabolic recovery following cessation.

Acknowledgments

The authors would like to express their sincere appreciation to all colleagues and staff who contributed to the successful completion of this study.

Conflict of Interest

None.

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