

# Evaluation of bony fractures in smokers using calcium ions and Alkaline phosphatase enzymes and supported with radiography

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## Abstract:

**Background:** smoking is considered as a major risk factor of bone fractures. This is attributed to decrease of serum calcium in smokers. Smokers are vulnerable to bone fractures more than non-smokers. **Aim of the study:** the study aims to assess the effect of smoking on patients involved with bone fractures. **Patients and methods:** the study was composed of 204 patients (smokers and nonsmokers). 78 smokers with bone fractures and 51 nonsmokers with bone fractures were interpreted. They were imaged with x-rays to diagnose the fractures. Biochemical procedure and measurements were performed to estimate serum calcium and alkaline phosphatase. **Results:** serum calcium is significantly decrease in fractured-bone smokers more than nonsmokers (p-value = 0.012), alkaline serum is significantly increased in smokers more than nonsmokers (p-value = 0.041). There was strong negative correlation between the levels of serum calcium and the number of cigarettes smoked per day (P-value = 0.016, R = 0.443). A strong negative correlation existed between the levels of serum calcium and the duration of smoking per years (P-value = 0.01, R = 0.42). A moderate positive correlation between the levels of serum calcium and the number of cigarettes smoked per day (P-value = 0.042, R = 0.277). **Conclusion:** smoking is an increased relative risk factor of bone fractures in Sudanese cigarette smokers. Bones of smokers were vulnerable to fractures more than non-smokers.

## Introduction

Fractures of bones are nowadays the major health problem in the world and particularly in the developing countries. Smoking is the most health issue that had been studied as it causes severe health problems. Many studies have demonstrated that smoking, and nicotine in particular, has direct effects on the health of bone and its ability to heal itself (1). Nicotine causes osteoblasts, the cells that make bone tissue, to be unable to function as well or grow as they normally would (2). That means bones of smokers are vulnerable to fractured more than nonsmokers. This means that when a smoker gets a fracture, it does not heal as well as the healthy one in a non-smoker. The bones take longer to heal and are weaker than those of non-smokers. Most importantly, smokers are more likely to have incomplete healing of the bone than are non-smokers (2). Most smokers are not

aware that smoking has serious effect on bones, joints and tissues; it mainly causes heart and respiratory diseases and leads to several cancers [3, 4, 5].

The study aims to analyze serum calcium and serum alkaline phosphatase in patients with fractures in order to study smoking effect. Several studies had demonstrated the effect of smoking on bone fractures and healing. The purpose of the study is to investigate the effect of smoking on acceptability of fractures which had been demonstrated with conventional radiography. The serum alkaline phosphatase and serum calcium levels had been estimated in smokers and nonsmokers to study the suspected changes in the control and test groups.

The radiography is the first line to assess the bones' fractures; types and classification. In this study the fractures were classified and mostly they were simple and compound. Therefore, x-rays application is valuable for classifying the fractures and for the monitoring of treatment after conservative surgical treatment. Among types of fractures, traumatic fractures were the most common types and results from accidents. Fractures may occur when the quality of bone is insufficient to handle the normal stress of weight bearing due to osteoporosis that had been found to be a common finding in smokers. Therefore, smoking increased the risk of fractures [6, 7].

### **Materials and methods:**

#### **Study design and population:**

This is a descriptive, case-control, cross-sectional study conducted in hospitals of Khartoum state in Sudan. The study population composed of 204 cigarette smokers and nonsmokers. Both the control group and the test group were matched in age and socioeconomic status. Interviews with the cigarette smokers and the controls were made to obtain the clinical data. A questionnaire was specifically designed to obtain information which helps in either including or excluding certain individuals in or from the study. Informed consent was taken from every patient.

Inclusion criteria include long standing cigarette smokers (10 years and more) were selected as a test group in this study. Exclusion criteria included those with parathyroid gland disease, renal disease, acute pancreatitis, malabsorption, bone disease and liver disease. These had been excluded from the study.

#### **Biochemical procedure and measurements**

Serum levels of calcium and alkaline phosphatase activity were measured using an auto analyzer. Instruments such as Roche Diagnostic/Hitachi 902 analyzer were used to measure and report the Serum levels of calcium and alkaline phosphatase activity. The following materials were used: plain containers, alcohol swabs, cotton, marker pens, and centrifuge, and saline (non-buffered), reagents, cleaning solution system, sample cups, printer paper, samples and reagent probes.

**Estimation of serum calcium:**

Calcium in the sample reacts with arsenazo, forming a coloured complex that can be measured. The linearity Range in this method is linear up to 18 mg/dl. The analyzer automatically adds equal quantities from the sample, R1 and R2 to the reaction.

**Estimation of serum alkaline phosphatase activity:**

Alkaline phosphatase catalyzes in alkaline medium the transfer of the phosphate group from 4nitrophenylphosphate to 2-amino-2-methyl-1propanol (AMP), liberating 4nitrophenol that can be measured at 405nm. Linear Range: This method is linear up to 1200 unit per liter (U/l). The analyzer automatically adds equal quantities from the sample, R1 and R2 to the reaction. The precision and accuracy of all methods used in this study were checked by commercially prepared control sera.

**Statistical Analysis:**

The data collected in this study were analyzed using SPSS 16. The means and standard deviation of the serum levels of calcium and alkaline phosphatase were obtained to both the test group and the controls and the t-test was used for comparison (p value of < 0.05 was considered to be significant). Linear regression analysis was used to asses correlation between the duration of cigarette smoking (in years), number of cigarettes smoked per day and the serum levels of the above variables.

**Radiographic procedure**

The patients had been investigated with conventional radiography using Toshiba x-ray unit. As most of patients had traumatic fractures, the majority of them were imaged in trolley immediately after the accident in the emergency department. Every fracture was imaged in two planes to evaluate the depth; anteroposterior (AP) and lateral projections. Alternative projections were taken if necessary. The exposure factors; kilovoltage (kV), milliampere (mA) and time were selected properly to demonstrate the fractures. Lead shields were used for protection. Patients were monitored carefully during the procedure.

**Results:**

The total target population of the study was composed of 204 smokers and non smokers. There were 78 of smokers had bones fractures, 51 non-smokers had bone fracture, 32 smokers had no bone fractures and 43 non-smokers without bone fracture as shown in table 1. There was significant difference between the two groups, p- value = 0.014. The serum calcium and serum alkaline phosphatase of patients with fractures had been analyzed and compared between smokers and non-smokers. Serum calcium was significantly decrease in smokers more than non-smokers (p-value = 0.012). But serum alkaline phosphatase showed significant increase in smokers more than non-smokers (p-value = 0.041), shown in table 2.

Distribution of ages according to the numbers of bone and non-bone fractures was shown in figure 1. Figure 2, 3 shows negative correlation between the levels of serum calcium and with both the number of cigarettes smoked /day and the duration of smoking / years. (P-value = 0.016, R = 0.443), (P-value = 0.01, R = 0.42) respectively. There was also

moderate positive correlation between the levels of serum alkaline phosphatase and with both the number of cigarettes smoked /day and the duration of smoking / years. (p- value = 0.042), R = 0.277), (P-value = 0.031, R = 0.192) respectively as shown in figure 4, 5.

Table (1) describes the number of the Bone and non-bone fracture smokers, P value and OD ratio.

Cases	Smokers		Non smokers		P. Value	OD ratio
Number & %	N	%	N	%		
Bone fracture	78	38	51	25	0.014	2.055
Non Bone fracture	32	16	43	21		
Total cases	204					

Table (2) Comparison of the means of serum calcium and alkaline phosphatase between the Bone fracture and the Non Bone fracture parameters.

Variable	Bone fracture (mean $\pm$ SD)		p-Value	Non Bone fracture (mean $\pm$ SD)		P-value
	Smokers	Non smokers		Smokers	Non smokers	
Serum calcium (mg/dl)	(7.36 $\pm$ 0.51)	(8.71 $\pm$ 0.72)	0.012	(10.73 $\pm$ 0.51)	(9.21 $\pm$ 0.42)	0.047
Serum alkaline phosphatase (u/L)	(116.06 $\pm$ 6.36)	(108.04 $\pm$ 5.05)	0.041	(98.16 $\pm$ 6.36)	(95.84 $\pm$ 5.05)	0.036

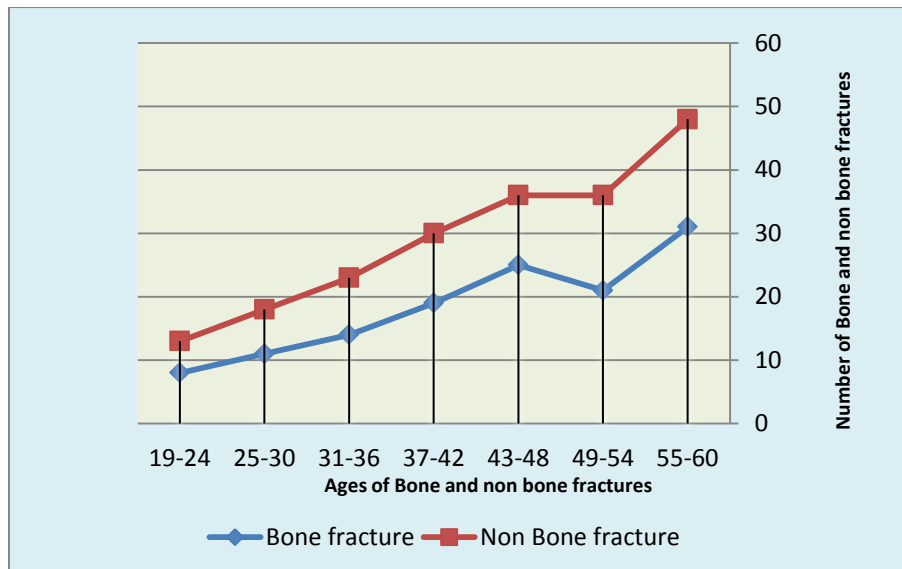
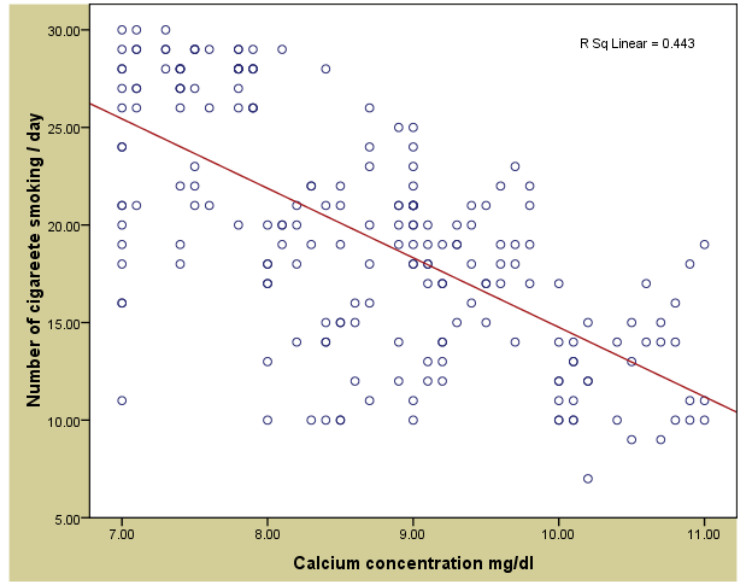
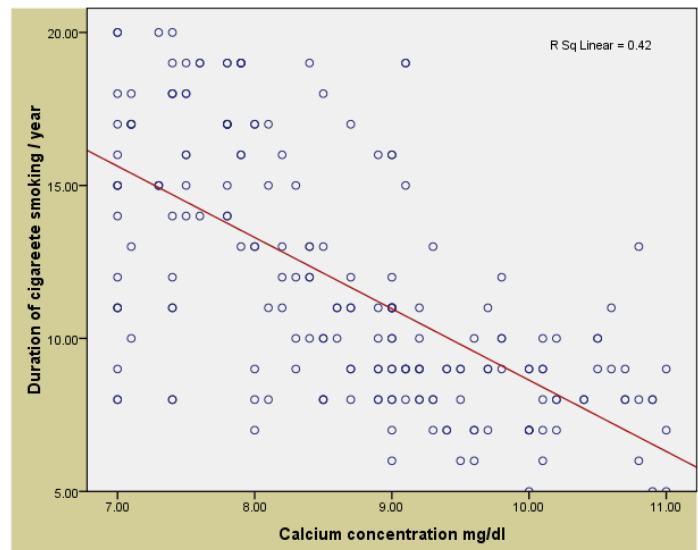


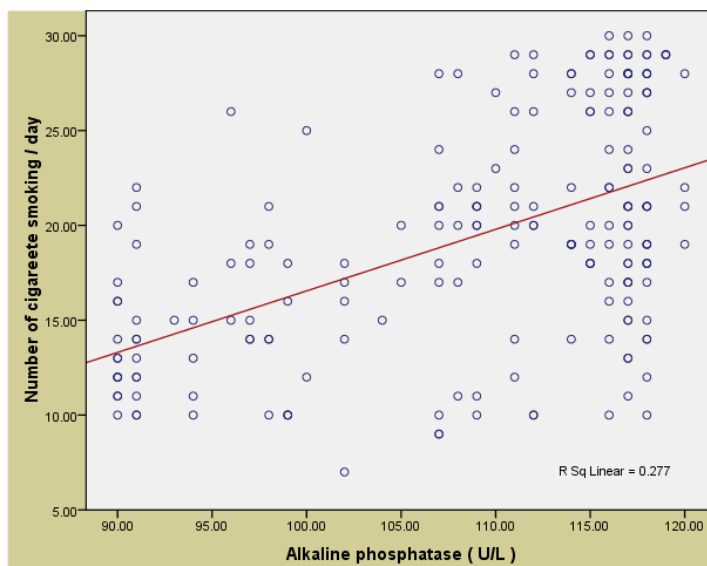
Figure (1): Distribution of the ages according to the number of Bone and non-bone fracture.



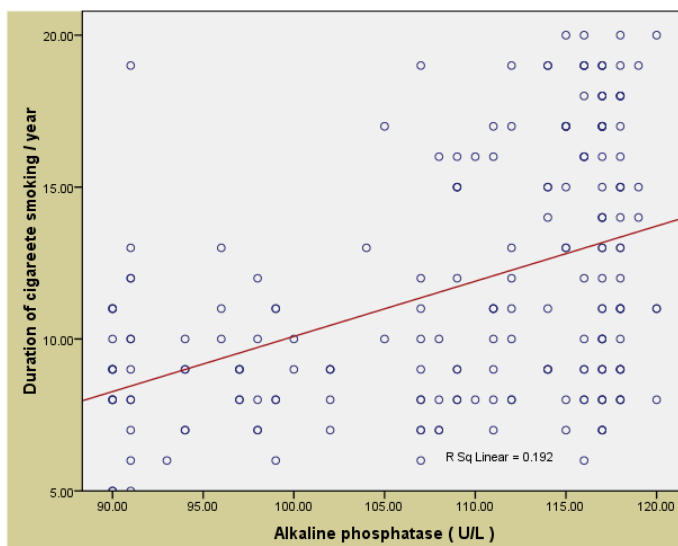
**Figure (2):** strong negative correlation between the levels of serum calcium and the number of cigarettes smoked /day. (P-value = 0.016, R = 0.443).



**Figure (3):** strong negative correlation between the levels of serum calcium and the duration of smoking / years. (P value = 0.01, R = 0.42).



**Figure (4):** moderate positive correlation between the levels of serum alkaline phosphatises and the number of cigarettes smoked /day. (P value = 0.042, R = 0.277).



**Figure (5):** moderate positive correlation between the levels of serum alkaline phosphatise and the duration of smoking / years (P value = 0.031, R = 0.192).

## Discussion

Serum calcium is regulated mainly by two hormones, the parathyroid hormone (PTH) and the active form of vitamin D<sub>3</sub> [1, 25 (OH)<sub>2</sub> vitD<sub>3</sub>]. The parathyroid hormone causes mobilization of calcium and phosphate from bone to plasma [8], while its action on the renal tubules is to enhance reabsorption of calcium and loss of phosphate. The overall action of PTH is to increase serum calcium and to reduce serum phosphate, but in the present study the reverse occurred. The active form of vitamin D<sub>3</sub> increases absorption of both calcium and phosphate in the intestine and also increases their reabsorption, in the renal tubules and hence, increases the level of serum calcium and phosphate in plasma. Therefore, any interference with the action of vitamin D may lead to decrease of serum calcium [9, 10].

The study showed that there was serum calcium significant reduction, while serum alkaline phosphatase was significantly increased in the cigarette smokers group, when compared to the non-cigarette smokers group.

According to the results of this study, serum calcium was observed to be affected with smoking. In the present study, serum calcium was negatively correlated with both; the number of cigarettes smoked per day and with the duration of the smoking. This indicates that smoking had negative adverse effect on bone density.

In this study, it was observed that serum alkaline phosphatase enzyme was significantly raised in the cigarette smokers and had a positive correlation with both; the duration of smoking and the number of cigarettes smoked per day. Increase of ALP enzyme activity could be due to increase activity of osteoblast that play a role in bone turnover and hence try to compensate for the low plasma calcium. This effect could be a cumulative effect of one or more of the chemicals in cigarette smoke may interfere with action of the PTH. This could be by inhibiting; its release from the parathyroid gland, its action on bone or its action on the renal tubules, that is reflected as lowering of serum levels of calcium and increasing of serum alkaline phosphatase. This correlated with the increasing of both; the duration of smoking and also with the number of cigarettes smoked per day. Our results concerning the levels of serum calcium in cigarette smokers, agrees with previous studies. A study done by Ramp et al on the levels of serum calcium in cigarette smokers in the UK [11, 12] and this result is consistent with our study finding.

Finally, the study concluded that smoking had an increased adverse effect on bone causing significant decrease in serum calcium which weakened the bones and lead to fractures at cigarette smokers more than non- smokers (ODD ratio = 2.055, P- value = 0.014).

**Conclusion:** In conclusion, smoking is an increased relative risk factor of bone fractures in Sudanese cigarette smokers. Bones of smokers were vulnerable to fractures more than non-smokers.

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