

Scientific research

University of Baghdad

Al-kindy college of medicine



CROSS SECTIONAL STUDY - THE PREVALENCE OF BONE FRACTURE AMONG SMOKERS ATTENDING TO AL-KINDY TEACHING HOSPITAL

The study submitted by:

Hussein Sabah Wadi

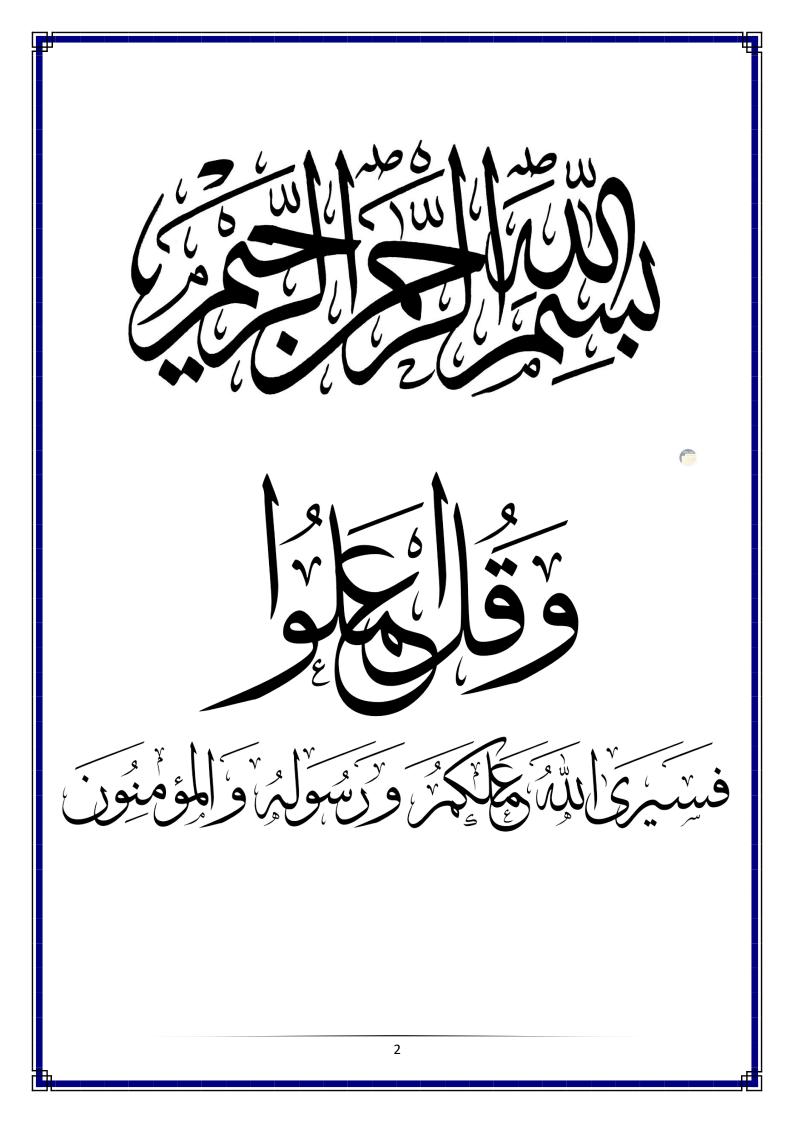
Ali Jabbar Fadhil

Temeam Mohammed Hussein

Hussein Hadi Salman

Supervised By:

Dr. Mohammed Shihab Ahmed



Contents	Page NO.
Abstract	4
Introduction	5
Aim	7
Methodology	8
Result	10
Discussion	14
Conclusion	16
Recommendation	16
Acknowledgment	17
References	18

List of tables	Page NO.
Table (1): Socio-demographics of the	10
sample.	
Table (2): Prevalence of fracture in the	10
study sample.	
Table (3): Sites of bone fractures.	11
Table (4): Prevalence of fracture	11
according to smoking categories.	
Table (5): Association between socio-	12
demographics & bone fractures.	
Table (6): Association between smoking	13
categories & bone fractures.	

Abstract:

Fractures are a major cause of morbidity and disability in older people, often leading to premature death. From 2006 to 2025, annual fracture events and costs for affected populations in the United States are projected to grow by more than 48%. Smoking has a negative impact on bone mineral density (BMD), reducing calcium absorption and lowering levels of vitamin D, changing hormone levels, and reducing body mass. Smoking is also associated with a higher risk of bone fracture, slower healing, and nonunion. In recent years, extensive studies have been conducted on the association between smoking and musculoskeletal disorders, confirming the existence of a causal relationship between tobacco smoking and osteoporosis, and fragility fractures.

Aim:

To view the prevalence of bone fractures among smokers

Methods:

A cross-sectional study was conducted among patients attending to Al-Kindy Teaching Hospital (KTH) during the academic year 2022-2023. A convenient sample with a sample size of **151** patients attending to Al-Kindy Teaching Hospital was collected.

The patients that were eligible to include <u>151 patients</u>. <u>Only 29 patients</u> were excluded due to exclusion criteria.

Using Excel, SPSS, and Tables for Numbering and making percentages for description.

Results:

A total of 151 participants from Al-kindy teaching hospital (KTH) participated in the study. Participants that had bone fracture in the study sample were **24.5%**. The prevalence of fracture is greater among the middle age group (**62.2% P-value** = 0.023). The prevalence of fracture was greater among heavy (Pack/Year) smokers, 17 patients out of a total of 37 (46%) had bone fracture/s (**P-value** = 0.001), **32.4%** were moderate smokers, and only 21.6% were light smokers.

Conclusion:

This study suggests that smoking is a dominating risk factor for fracture.

Introduction:

Fractures are a major cause of morbidity and disability in older people, often leading to their premature death [1]. As the global population ages, fractures are expected to increase significantly in the coming decades [2]. Worldwide, the number of people aged 50 years or older, and who were at high risk of fracture was around 158 million in 2010, and that number is expected to double by 2040. In the United States, data from 2013–2014 indicated that around 8.3% of adults should have received treatment because they were at a 20% or greater 10-year risk of fractures. From 2006 to 2025, annual fracture events and costs for affected populations in the United States are projected to grow by more than 48% [2]. Thus, fracture prevention is essential for both high-risk individuals and for society in general.

Fractures occur in individuals of all ages. However, the type and body location vary widely depending on different factors, mainly related to individual bone quality and the nature of the trauma. Especially for the fractures occurring in the elderly population, which are often fragility fractures. The World Health Organization (WHO) has described fragility fractures as fractures that result from mechanical forces that would not normally lead to a fracture. The incidence of fractures in many body locations have been reported to increase [3]. Which mainly could be attributed to an increase in numbers of fragility fractures in a growing elderly population [4]. Many factors may contribute to changes in the incidence rates—such as comorbidities of diabetes, obesity, smoking and others, the use of certain medications; mental factor and social factors [5].

The World Health Organisation indicate that injury is a substantial cause of morbidity and mortality in low- and middle-income countries (LMICs) [6]. Some studies have indicated that road traffic accidents cause 68.14% of fractures in some LMIC countries. Falls are also a serious public health problems worldwide because they can also cause re-injury. Some studies have demonstrated that falls have a prevalence of 21.8% and 35.1%. Over the last several years, long bone fractures are becoming increasingly common. More than 90% of injuries, particularly fractures of the extremity, occur in LMICs. As the standard of health and lifestyle improves in LMICs, one can expect that the older population, who are more prone to falls and fractures, will be greatly affected. Therefore, the burden is expected to rise substantially [7].

The burden of long bone fractures impacts society through the loss of productivity, the direct and indirect costs of treatment and the additional contribution to morbidity and mortality. The management and treatment of long bone fractures add significantly to the expenses of any health care system because of the cost of surgery, possible rehospitalisation and the physical rehabilitation of patients [8].

Smoking is the single most preventable cause of disease, disability, and death in the United States. Recent data suggested that there are still approximately 34.2 million adult smokers in this country [9]. Specifically, men are more likely to smoke than women in the US since 16.7% of adult males and 13.6% of adult females smoke cigarette [10]. In addition, smoking accounted for an estimated 3.1 million years of potential life lost for male smokers and 2.0 million years for female smokers during 2000-2004. Suggesting that men are at higher risk of smoking-related conditions than women [11]. Moreover, Experts estimate that 16 million Americans live with a disease caused by smoking. Every year, roughly 480,000 people die from smoking-related diseases. That means that for every person who dies from smoking, at least 30 others live with a serious smoking-related illness.

Researches continue to pinpoint more ways tobacco harms your health, from cancers to chronic (long-term) diseases [12].and by the 1990s, it was known that smoking causes harm to the entire musculoskeletal system [13-16].

Smoking has a negative impact on bone mineral density (BMD), reducing calcium absorption and lowering levels of vitamin D, changes hormone levels, and reduces body mass[17].Smoking is also associated with a higher risk of bone fracture, slower healing, and nonunion.

extensive studies have been conducted on the association between smoking and musculoskeletal disorders, confirming the existence of a causal relationship between tobacco smoking and rheumatoid arthritis, periodontitis, osteoporosis, and fragility fractures. This association is related to the effects of smoking on imbalances in bone turnover, with a consequent increase in bone fragility [18]. Moreover, study has shown how long-term smoking is associated with a decline in muscle functionality and sarcopenia [19].

Prior studies found that smoking was associated with a significantly increased risk of fractures [20]. Smoking increases the risk of spine and hip fracture to 32% and 40% in men, respectively [21]. The one-year mortality rates were as high as 20.6%, and 37.1% [22] among male smokers with spine and hip fractures. Hence, a reliable estimate of the association between smoking and fractures in men is crucial, which might help to improve their recognition of the dangers of smoking.

The recognition that certain lifestyle behaviors can increase fracture risk in later life for both men and women has recently received increasing attention. Recent studies link smoking to low bone density in women by a variety of factors attributable to smoking: early menopause, thinness, reduced circulating estrogens, and decreased calcium absorption [23]. Other studies associating bone loss with smoking, mostly in older men, have also been reported [24-28]. In addition, Valimaki et al. observed a relationship between low bone density and smoking during adolescence and early adulthood [29].

However, some reports suggest a lack of association between smoking and bone density [30]. Additional studies are needed to clarify the relationship of the effects of smoking duration, quantity smoked, and past cigarette use on bone density and prospective bone loss rates. The prevalence of male osteoporotic fractures constitutes a serious clinical problem with significant economic consequences. In several meta-analyses, smoking has been recognized as a risk factor for low bone mineral density (BMD) and increased risk of hip fracture [31].

Aim of the study:

To view the prevalence of bone fractures among smokers.

Methodology:

A cross-sectional study was conducted among patients attending to al-Kindy Teaching Hospital (KTH) during the academic year 2022-2023.

A convenient sample was collected during the period from 14th of November 2022 to 10th January 2023. The sample size was 151 patients from KTH. Using Self-administered questionnaire, and included 11 questions. The questionnaires had two parts. Part one is demographical data that include age, and gender. Part two includes information about current or previous bone fracture/s, the date, site, and cause of the fracture, and any bone-related diseases, and information about smoking status, duration, amount (pack/day), and type of smoking.

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 29.0.1. We used Excel, SPSS and Tables for Numbering and making percentages for description.

Inclusion criteria of the sample include:

- Age: between 20 to 65 years.
- Smoking duration at which the fracture/s occurs is more than 5 years. (Smoker for 5 years at least, before the fracture occurs).

Exclusion criteria of the sample include:

- Road traffic accidents.
- Patients with a history of bone-related diseases.
- The patients that were eligible to include was <u>151 patients</u>. <u>Only 29 patients</u> were excluded due to exclusion criteria.

Variables definition:

Exposure: Smoking.

Outcome: Bone Fracture.

Confounders:

- Post-menopause women.
- Calcium intake.
- Vitamin D intake.
- Physical activity.
- Alcohol consumption.
- Drugs.
- bone mineral density (BMD).
- body mass index (BMI).

Age was categorized into three categories. Young (between 20-40 years old), Middle (Between 40-60 years old), and Elderly (>60 years old).

We converted the smoking of electronic cigarettes, Vape and Argela into cigarettes packs by using the following formula:

2 milliliters of electronic cigarette, Vape and argela juice = 1 Pack of Cigarettes.

The duration of smoking was categorized into 3 categories. Light (5-10 years), moderate (10-30 years), heavy (more than 30 years).

The dose of smoking was categorized into 3 categories. Light (1 pack or less per day), Moderate (more than 1 and less than 2 packs per day), heavy (3 packs per day or more).

Pack/Year was calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked, by mean using the following formula:

Pack/Year = Packs (per day) x Smoking Duration (Years)

Pack per/year Smoking was categorized into three categories. Light smoker (less than 20 pack/year), Moderate smoker (between 20-40 pack/year), and Heavy smoker (more than 40 pack/year).

Results:

A total of 151 participants from Al-kindy teaching hospital (KTH) participated in the study 45.7% of them were between 20-40 years, 43% of them were between 40-60 years, and 11.3% were more than 60 years old. The mean age of participants was 43.25 ± 12 . In addition, 67.5% of participants were males and 32.5% were females. **(Table 1)**

Var	No.	%	
Age (yrs.)	20-40	69	45.7
	40-60		43
	>60	17	11.3
Gender	Female	49	32.5
	Male	102	67.5

Table (1): Socio-demographics of the sample:

Young age <40 years, middle age 40-60 years, elderly >60 years.

Regarding participants that had a bone fracture in the study sample were 24.5%. **(Table 2)**

Table (2): Prevalence of fracture in the study sample:

Fracture	No.	%
No	114	75.5
Yes	37	24.5
Total	151	100

Regarding participants that had a bone fracture, Hip fractures were 32.4%, Leg fractures were 21.6%, Forearm fractures were 18.9% and other bone fractures (Small bones fracture, Rip fracture, Vertebral fracture ..etc.) were 27.1%. (Table 3)

	NO.	%
Forearm	7	18.9
Hip	12	32.4
Leg	8	21.6
Other	10	27.1
Total	37	100

Table (3): Sites of bone fractures:

Of the 151 participants in the study. We found that 68 (45%) of them were light (pack/year) smokers, with 8 (21.6%) of these 68 light smokers have had bone fracture/s. Moderate (pack/year) smokers were 43 (28.5%), with 12 (32.4%) of these 43 moderate smokers have had bone fracture/s. Heavy (pack/year) smokers were 40 (26.5%), with 17 (46%) of these 40 heavy smokers have had bone fracture/s. **(Table 4)**

Table (4): Prevalence of fracture according to smoking categories:

		Fracture					
			No	Yes		Total	
		NO.	%	NO.	%	NO.	%
Pack/Year	Light	60	52.6	8	21.6	68	45
	Moderate	31	27.2	12	32.4	43	28.5
	Heavy	23	20.2	17	46	40	26.5
Duration of	Light	36	31.6	3	8.1	39	25.8
smoking	Moderate	64	56.1	20	54.1	84	55.7
	Heavy	14	12.3	14	37.8	28	18.5
Dose of	Light	69	60.5	12	32.4	81	53.6
smoking	Moderate	9	7.9	6	16.2	15	9.9
	Heavy	36	31.6	19	51.4	55	36.5

In the study, we found that there is an association between age and bone fracture. That the prevalence of fracture is greater among the middle age group (62.2%) P-value = 0.023 (chi-square test). There was no association between the gender of the participants and the smoking P-value = 0.688 (chi-square test). (Table 5)

Varia	Variables		Patients with fractures	
		No.	%	P-value
Age (yrs.)	20-40	12	32.4	
	40-60	23	62.2	0.023*
	>60	2	5.4	
Gender	Female	13	35.1	0.688
	Male	24	64.9	

Table (5): Association between socio-demographics & bone fractures.

*The chi-square statistic is significant at the 0.05 P. value

There was a significant association between bone fractures and smoking categories. The prevalence of fracture was greater among heavy (Pack/Year) smokers, 17 patients out of a total of 37 (46%) had bone fracture/s (P-value = 0.001), 32.4% were moderate smokers, and only 21.6% were light smokers.

Also, it was greater in the moderate (duration of smoking) category 54.1% (P-value = ≤ 0.001), 37.8% were heavy smokers, and only 8.1% were light smokers.

Furthermore, it was greater in the Heavy (Dose of Smoking) category at 51.4% (P-value = <u>0.011</u>), 32.4% were light smokers and only 16.2% were moderate smokers. (Table 6)

Table (6): Association between smoking categories & bone fractures.

variables	category	Fracture			
		NO.	%	P value	
	Light	8	21.6		
Pack/Year	Moderate	12	32.4	0.001*	
	Heavy	17	46		
Duration of smoking	Light	3	8.1		
	Moderate	20	54.1	<0.001*	
	Heavy	14	37.8		
Dose of smoking	Light	12	32.4		
	Moderate	6	16.2	0.011*	
	Heavy	19	51.4		

*The chi-square statistic is significant at the 0.05 P. value

Discussion:

This cross-sectional study shows an increase in the prevalence of bone fracture among smokers attending to Al-Kindy Teaching Hospital. Prevalence of bone fractures was significantly higher in heavy smokers (pack/year) and (dose of smoking), 46% (p-value=0.001) and 51.4% (p-value=0.011) respectively. Also, it was significantly higher in moderate smokers according to the duration of smoking 54,1% (p-value=<0.001). (Table 6)

The dose-effect increase in bone fracture with greater cigarette consumption suggests that smoking as a risk factor for bone fractures, and that supported by previous studies [32], they found that In current smokers, there was a positive linear relationship between daily tobacco consumption and overall fracture risk as well as the risk of hip fracture. The overall fracture risk increased by 30%, and the risk of hip fracture by 50%, per every 5-g increase in tobacco smoked, which might indicate that smoking dose is even more important for hip fracture than for the overall fracture risk in men. Previous studies generally only have data on cigarettes, and an elevated risk of hip fracture was revealed in those smoking at least one pack of cigarettes each day or at least 15 cigarettes each day. Only Höidrup et al. [33] have presented data on the total amount of tobacco smoked in grams (dichotomized ± 15 g/day) and showed a significantly increased risk of hip fracture for the high-dose category, and found that smoking cessation leads to a decline in the risk of hip fracture in previous smokers almost reversed 5 years after smoking cessation. The benefits of smoking cessation may be exaggerated if former smokers have less cumulative exposure to tobacco than continuing smokers [33].

In our study, we find that the duration of smoking was significantly associated with an increased risk of bone fracture but In Höidrup et al. Study Smoking duration showed no increase in fracture risk, in either current or former smokers, which was also supported by previous studies where smoking duration conferred no additional risk of hip fracture, at least not in men [33], this difference is not clearly known why.

Other meta-analysis study [34] found that the effect of smoking is over and above that which can be explained by variations in BMD. The risk of subsequent fractures was greater in the case of hip fracture than for all fractures, and intermediate for osteoporotic fractures. For hip-fracture risk in women, the increase in risk ratio (1.85) was comparable to that described in the meta-analysis from Law and Hackshaw [35]. In this study, they find the risk ratios for osteoporotic fractures (which included hip fractures) increased with age. The strength of the association they find was lower than for ever-smokers, consistent with the view that the effect of smoking appears to wane slowly after a person stops smoking.

In another large, prospective study from Kuopio, the risk of fracture for current smokers was 1.47 (95% CI=1.05–2.06) when the sample included individuals selected on the basis of risk factors. From the random population sample, the relative risk for fractures overall was 1.18 (95% CI=0.70–2.00) [36].

Although the gender was not associated with increased risk of fractures but the bone loss is reported to be higher in male smokers than in female smokers, perhaps due to men's higher exposure to cigarette smoking. Is some study they observed higher risk ratios for men (64.9%) than for women (35.1%) for any fracture. However, as shown in the present study, this represents a minority of the risk.

Also, in our study, we find that the increased age was associated with a higher prevalence of bone fractures. Confirmed reports [34] that cigarette smoking is a risk factor for hip fractures. Their results are in agreement with those from a recent meta-analysis [35] in which a 17% increased risk of hip fracture was reported for current smokers compared with nonsmokers at age 60.

Several mechanisms might explain the increased risk of bone fracture among smokers. Smoking alters the metabolic pathway of estradiol in the liver in that more estrogen is converted to its inactive compound [38]. It also induces the liver cytochrome P-450 enzyme system [39]. Smokers are also thinner and, hence, have lower body mass index. Consequently, the protective effect of adipose tissue and peripheral estrogen metabolism is impaired. The observations that estrogen is less effective in protecting smokers against bone fracture [40]. Smokers also have lower fractional absorption of calcium [41].

Study limitations:

A limitation of our study is that we could not measure bone mineral density (BMD) which is used to identify normally and decreased bone mass. We were also limited by the measurements of the levels of calcium and vitamin D in our participants, postmenopausal estrogen therapy, lack of physical activity or taking some medications such as non-steroidal anti-inflammatory drugs (NSAID).

Finally, it is possible that there is residual confounding from factors that were not assessed in this study.

Conclusion:

This study suggests that smoking is a dominating risk factor for fracture, the risk depends both on the recency of smoking and on the daily amount of tobacco smoked, and this risk factor is also modifiable. Furthermore, our results suggest a more long-lasting negative effect of smoking on fracture risk than has been estimated by earlier studies.

Recommendations:

The risk of fracture among current smokers can be substantially reduced by decreasing the amount of tobacco smoked, people who smoke and their physicians should consider smoking cessation as a nonpharmacological approach to reducing the risk of bone fracture.

Numerous studies showed that during the first 10 years after cessation, the risk of fracture was reduced, indicating that quitting smoking could prevent fractures .

The increased fracture risk with smoking was stronger than has previously been estimated in studies without time-dependent exposure and covariate analyses. This analytical approach might be considered when possible in all prospective longitudinal studies for other time-varying exposures such as diet and physical activity.

Acknowledgment:

The authors are very thankful to all who participate in this study, also the authors are obligated to thank Dr. Muhammad Shihab Al-Edani, assistant of the brigadier general for his supervision of the entire study, and the department of family and community of Al-kindy medical college for their very kind cooperation.

References:

1- Colón-Emeric, C. S. & Saag, K. G. Osteoporotic fractures in older adults. Best Pract. Res. Clin. Rheumatol. 20, 695–706. (2006).

2-Burge, R. et al. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025. J. Bone Miner. Res. 22, 465–475 (2007).

3-Beerekamp MSH, de Muinck Keizer RJO, Schep NWL, Ubbink DT, Panneman MJM, Goslings JC. Epidemiology of extremity fractures in the Netherlands. Injury. 2017;48(7):1355–62.

4-Hernlund E, Svedbom A, Ivergard M, Compston J, Cooper C, Stenmark J, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). Archives of osteoporosis. 2013;8:136.

5-Court-Brown CM, Clement ND, Duckworth AD, Biant LC, McQueen MM. The changing epidemiology of fall-related fractures in adults. Injury. 2017;48(4):819–24.

6-Haagsma JA, Graetz N, Bolliger I, et al. The global burden of injury: Incidence, mortality, disability-adjusted life years and time trends from the Global Burden of Disease study 2013. Inj Prev. 2016;22(1):3-18.

7-Manwana ME, Mokone GG, Kebaetse M, Young T. Epidemiology of traumatic orthopaedic injuries at Princess Marina Hospital, Botswana. SA Orthop J. 2018;17(1):41-46.

8-Pasco JA, Lane SE, Brennan-Olsen SL, et al. The epidemiology of incident fracture from cradle to senescence. Calcif Tissue Int. 2015;97(6):568-576.

9-Creamer, M. R. et al. Tobacco product use and cessation indicators among adults — United States, 2018. MMWR Morb. Mortal. Wkly. Rep. 2019 68, 1013–1019 (2019).

10-Jamal, A. et al. Current cigarette smoking among adults – United States, 2005–2015. MMWR Morb. Mortal. Wkly Rep. 65, 1205-1211 (2016).

11- Adhikari, B., Kahende, J., Malarcher, A., Pechacek, T. & Tong, V. Smoking-attributable mortality, years of potential life lost, and productivity losses. Oncol. Times 31, 40–43 (2009).

12-Parascandola M. Skepticism, statistical methods, and the cigarette: a historical analysis of a methodological debate. Perspect Biol Med 2004;47:244-261.

13-Reynolds KL, Heckel HA, Witt CE, et al. Cigarette smoking, physical fitness, and injuries in infantry soldiers. Am J Prev Med 1994;10:145-150.

14-Leigh JP. An empirical analysis of self-reported, work-limiting disability. Med Care 1985;23:310-319.

15-Mäkelä M, Heliövaara M, Sievers K, et al. Musculoskeletal disorders as determinants of disability in Finns aged 30 years or more. J Clin Epidemiol 1993;46:549-559.

16-Hubert HB, Fries JF. Predictors of physical disability after age 50. Six-year longitudinal study in a runners club and a university population. Ann Epidemiol 1994;4:285-294.

17-Seeman E, Melton LJ, III, O'Fallon WM, Riggs BL. Risk factors for spinal osteoporosis in men. Am J Med 1983;75:977-983.

18-Ward, K.D.; Klesges, R.C. A meta-analysis of the effects of cigarette smoking on bone mineral density. Calcif. Tissue Int. 2001, 68, 259–270.

19-Morse, C.I.; Wüst, R.C.I.; Jones, D.A.; de Haan, A.; Degens, H. Muscle fatigue resistance during stimulated contractions is reduced in young male smokers. Acta Physiol. 2007, 191, 123–129.

20-Meyer, H. E., Tverdal, A. & Falch, J. A. Risk factors for hip fracture in middle-aged Norwegian women and men. Am. J. Epidemiol. 137, 1203–1211.(1993).

21-Ward, K. D. & Klesges, R. C. A meta-analysis of the effects of cigarette smoking on bone mineral density. Calcif. Tissue Int. 68, 259–270 (2001).

22-Kannegaard, P. N., van der Mark, S., Eiken, P. & Abrahamsen, B. Excess mortality in men compared with women following a hip fracture. National analysis of comedications, comorbidity and survival. Age Ageing 39, 203–209.(2010).

23-Dawson-Hughes B, Krall EA, Harris S 1993 Risk factors for bone loss in healthy postmenopausal women Osteoporos Int Suppl 1:S27–S31.

24-May H, Murphy S, Khaw KT 1994 Cigarette smoking and bone mineral density in older men QJM 87:625–630.

25-Mellstrom D, Rundgren A, Jagenburg R, Steen B, Svanborg 1982 Tobacco smoking, aging and health among the elderly: A longitudinal population study of 70 year old men and age cohort comparison Age Aging 11:45–58.

26-Nguyen TV, Kelly PJ, Sambrook PN, Gilbert C, Pocock NA, Eisman JA 1994 Lifestyle factors and bone density in elderly: Implications for osteoporosis prevention J Bone Miner Res 9:1339–1346

27-Rundgren A, Mellstrom D 1984 The effect of tobacco smoking on the bone mineral content of the aging skeleton Mech Aging Dev 28:273–277.

28-Slemenda CW, Christian JC, Reed T, Reister TK, Williams CJ, Johnston CC Jr 1992 Long-term bone loss in men: Effects of genetic and environmental factors Ann Intern Med 117:286–291.

29-Valimaki MJ, Karkkainen M, Lamberg-Allardt C, Laitinen K, Alhava E, Heikkinen J, Impivaara O, Makela P, Palmgren J, Seppanen R 1994 Exercise, smoking, and calcium intake during adolescence and early adulthood as determinants of peak bone mass: Cardiovascular Risk in Young Finns Study Group Br Med J 309:230–235.

30-Kroger H, Laitinen K 1992 Bone mineral density measured by dual-energy X-ray absorptiometry in normal men Eur J Clin Invest 22:454–460.

31-Kanis JA, Johnell O, Oden A, et al. Smoking and fracture risk: a meta-analysis. Osteoporos Int. 2005; 16: 155–162.

32- Helena Olofsson, Liisa Byberg, Rawya Mohsen, Hakan Melhus, Hans Lithell, and Karl Michaëlsson. Smoking and the Risk of Fracture in Older Men. 2005 Jul;20(7):1208-15.

33-Höidrup S, Prescott E, Sörensen TIA, Gottschau A, Lauritzen JB, Schroll M, Grönbaek M 2000 Tobacco smoking and risk of hip fracture in men and women. Int J Epidemiol **29:**253–259.

34-J. A. Kanis, O. Johnell, A. Oden, H. Johansson, C. De Laet, J. A. Eisman, S. Fujiwara, H. Kroger E. V. McCloskey, D. Mellstrom, L. J. Melton, H. Pols J. Reeve, A. Silman, A. Tenenhouse Smoking and fracture risk: a meta- analysis. 2005 Feb;16(2):155-62.

35- Law MR, Hackshaw AK.Ameta-analysis of cigarette smoking, bone mineral density and risk of hip fracture: recognition of a major effect. *BMJ*. 1997;315:841–846.

36-Huopio J, Kroger H, Honkanen R, Saarikoski S, Alhava E (2000) Risk factors for perimenopausal fractures: a prospective study. Osteoporos Int 11:219–227.

37-Jacques Cornuz, MD, MPH, Diane Feskanich, ScD, Walter C. Willett, MD, DrPH, Graham A. Colditz, MD, DrPH Smoking, Smoking Cessation, and Risk of Hip Fracture in Women. 1992 May 1;116(9):716-21.

38-Michnovicz JJ, Hershcopf RJ, Naganuma H, et al. Increased 2-hy- droxylation of estradiol as a possible mechanism for the anti-estro- genic effect of cigarette smoking. NEJM. 1986;315:1305–1309.

39-ConneyAH. Pharmacological implications of microsomal enzyme induction. Rev. 1967;19:317–366.

40-Kiel DP, Baron JA, Anderson JJ, et al. Smoking eliminates the pro- tective effect of oral estrogens on the risk for hip fractures among women. Ann Intern Med. 1992;116:716–721.

41-Krall EA, Dawson-Hughes B. Smoking and bone loss among post- menopausal women. J Bone Miner Res. 1991;6:331–337.