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Zinc and Magnesium Levels in Osteoporotic Patients from Northern Gaza Strip

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Abstract

Osteoporosis is a systemic disease of the skeleton, characterized by low bone mass and alterations in the micro-architecture of the bone tissue that lead to an increase in brittleness with the ensuing predisposition to bone fractures. To determine zinc and magnesium levels in osteoporotic northern Gaza patients and control groups. A case-control study included 40 osteoporotic patients and 40 controls aged 40-65 years. Magnesium and zinc levels were measured in the serum at Palestinian Medical Relieve Society-Gaza by absorption spectrophotometry method-XLFS Kit (Diasys Diagnostic System GmbH). In the present study serum zinc level in the control and in osteoporosis patients were ($83.0 \pm 17.3 \text{ mg/dl}$ and $73.8 \pm 20.3 \text{ mg/dl}$) respectively, and serum magnesium level in the control and in osteoporosis patients were ($1.9 \pm 0.22 \text{ mg/dl}$ and $1.8 \pm 0.34 \text{ mg/dl}$) respectively. Zinc and magnesium levels were significantly ($p < 0.05$) lower in patients than controls. The results of the present work indicated a positive role of sex, hormonal therapy, sex, and Locomotors activity in osteoporosis. Zinc and magnesium levels in the serum are significantly lower in postmenopausal women and men with osteoporosis than control subjects. It is concluded that low levels of zinc and magnesium may play a role in osteoporosis.

Keywords:

Osteoporosis,
Zink,
Magnesium.

1. Introduction:

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fractures (Srivastava et al., 2002). Osteoporosis is a condition in which an increased risk of fracture takes place due to a reduction of bone mineral content. It occurs as a result of unbalance between bone formation and bone resorption (Odabasi et al., 2008). Osteoporosis is classified into primary and secondary ones. Primary

osteoporosis is manifested by deterioration of bone mass that is unassociated with other chronic illness and is related to aging and decreased gonadal function. Therefore, early menopause or perimenopause estrogen deficiency states may hasten the development of primary osteoporosis. Prolonged periods of inadequate calcium intake, sedentary lifestyle and tobacco and alcohol abuse also contribute to this condition. Osteoporosis usually does not have an effect on people until they are 60 or older. Women are usually affected at

an earlier age than men, because they start out with lower bone mass (Bandeem-Roche et al., 2006). Secondary osteoporosis results from chronic conditions that contribute significantly to accelerated bone loss. These chronic conditions include thyroxin excess, hyperparathyroidism, malignancies, gastrointestinal diseases, medications, renal failure and connective tissue diseases (Brufsky et al., 2007). The disability mortality, and cost of hip and vertebral fractures are substantial in the rapidly growing, aging population so that prevention and treatment of osteoporosis is a major public health concern (Srivastava and Deal, 2002). Spinal deformities such as a stooped posture or Kyphosis can be a symptom of osteoporosis. A hunchback is the result of multiple vertebral compression fractures in the spine due to loss of bone mass (Rose et al., 2007). Risk factors can be categorized as modifiable, inadequate exercise, inadequate nutrition, calcium, vitamin D, smoking, alcohol abuse, medications, glucocorticoids, benzodiazepines, anticonvulsants, thyroid hormones and non-modifiable age, gender, race, early menopause, family history of fractures (Srivastava and Deal, 2002).

Osteoporosis affects millions people worldwide, predominantly postmenopausal women. (Castiglioni et al., 2013). Prevalence of the disease is increased in the world wide particularly in woman. Woman older than 45 years are more susceptible to osteoporosis, over 50 percent of women and 13 percent of men over age 50 will sustain an osteoporotic-related fracture. The increase of life expectancy and so the old age in the society in developing countries such as the Middle East has led to an increase in the prevalence of osteoporosis and its following fractures (Memon et al., 1998).

In recent years, there has been a resurgence of interest in studies concerning the role of elements in the development and maintenance of the skeleton (Razmandeh et al., 2014).

Trace element: such as iron, magnesium, manganese, zinc, copper, and iodine, are affected in osteoporosis individuals. Magnesium (Mg) appears to be important in bone cell activity. It is shown to be mitogenic for osteoblasts and its depletion causes cellular growth inhibition, in vitro. Zinc (Zn) is an essential mineral that is a component of more than 200 enzymes and is known to be necessary for normal collagen synthesis and mineralization of bone (Odabasi et al., 2008). Bone health is supported by many factors, most notably calcium and vitamin D. However, some evidence suggests that magnesium deficiency may be an

additional risk factor for postmenopausal osteoporosis. This may be due to the fact that magnesium deficiency alters calcium metabolism and the hormones that regulate calcium. Decreased serum magnesium levels have been found in postmenopausal patients with osteoporosis. Magnesium testing can be used effectively to help identify a woman's risk of osteoporosis (Reginster et al., 1989). Low serum zinc levels and excessive urinary zinc excretion appears to be related to osteoporosis. The elderly population may be at higher risk of zinc deficiency (Relea et al., 1995). Stendig-Lindberg and others investigated the effect of magnesium treatment on bone density in postmenopausal osteoporosis. Thirty-one postmenopausal patients and bone density values of $\sim 1.19\text{g/cm}^3$ received two to six tablets daily of 125 mg each of magnesium hydroxide (Magnesium Magma USP*; Mazon' Israel) for 6 months and two tablets for another 18 months in a 2 year open controlled therapeutic trial. Twenty-three symptom-free postmenopausal women whose bone density was concurrently assessed at the same laboratory' and who were found to have osteoporosis but refused treatment, served as controls. No new fractures occurred. Twenty-two patients (71 per cent) responded by a 1-8 per cent rise of bone density. The mean bone density of all treated patients increased significantly after 1 year ($P < 0.02$) and remained unchanged after 2 years ($P > 0.05$). The mean bone density of the responders increased significantly both after one year ($P < 0.001$) and after 2 years ($P < 0.02$), while in untreated controls the mean bone density decreased significantly ($P < 0.001$). The disparity between the Initial mean bone density and bone density after one year in all osteoporotic patients and in the responders differed significantly from that of the controls (both $P < 0.001$). In 5/31 treated patients (16 per cent) bone density remained unchanged. Suggesting an arrest of bone loss, thus in a total of 27/31 patients (87 per cent) there was either an increase of bone density or arrest of bone loss. (Stendig-Lindberg et al., 1993).

Serum concentrations of magnesium, zinc and copper were measured in postmenopausal women with osteoporosis ($n = 40$), osteopenia ($n = 40$) or normal bone mineral density ($n = 40$) as classified on the basis of the T-score of the femur neck and dual energy X-ray absorptiometry results. Mean concentrations of magnesium and zinc were significantly lower in osteoporotic women than in both osteopenic women and normal women. There were no statistically

significant differences observed between the osteopenic, osteoporotic and control groups with respect to copper levels (Mutlu et al., 2007). Odabasi and others measured magnesium (Mg), zinc, copper, manganese, and selenium by atomic absorptions spectrophotometry in both postmenopausal women with osteoporosis and healthy postmenopausal women. Only statistically significant difference between the osteoporotic (51.51 [15.40] $\mu\text{g}/\text{mL}$) and healthy subjects (54.54 [15.42] $\mu\text{g}/\text{mL}$) was observed in red blood cell (RBC) magnesium concentration ($Z = -2.07$, $P = 0.039$) (Odabasi et al., 2008). The independent association between dietary zinc and plasma zinc and the association of each with bone mineral density (BMD) and 4-y bone loss in community well in older men is examined. The mean dietary zinc intake was 11.2 mg, and the mean plasma zinc concentration was 12.7 $\mu\text{mol}/\text{L}$. Plasma zinc was correlated with total zinc intake (diet plus supplements). Dietary zinc intake and plasma zinc concentrations were lower in men with osteoporosis at the hip and spine than in men without osteoporosis at those locations. BMDs for the hip, spine, and distal wrist were significantly lower in men in the lowest plasma zinc quartile ($\sim 11.3 \mu\text{mol}/\text{L}$) than in men with higher plasma zinc concentrations. The association between plasma zinc and BMD was cross-sectional, longitudinal, and independent of age or body mass index. However, plasma zinc did not predict bone loss during the 4-y interval (Hyun et al., 2004).

Mahdaviroshan and others assessed the effect of zinc supplementation on serum zinc and calcium levels in postmenopausal osteoporotic women. Mean serum zinc concentrations were markedly lower than the normal range at baseline, but mean serum calcium levels were normal. In the intervention group serum zinc levels were significantly higher after 60 days [120.5 (SD 7.5) versus 70.5 (SD 4.6) $\mu\text{g}/\text{dL}$] while serum calcium levels were unchanged [8.6 (SD 0.1) versus 9.1 (SD 0.3) mg/dL]. The placebo group showed no significant changes in zinc or calcium levels. Postmenopausal osteoporotic women may benefit from zinc supplementation (Mahdaviroshan et al., 2012). Both low and high magnesium have harmful effects on the bones. Magnesium deficiency contributes to osteoporosis directly by acting on crystal formation and on bone cells and indirectly by impacting on the secretion and the activity of parathyroid hormone and by promoting low grade inflammation. Less is known about the mechanisms responsible for the mineralization defects observed when magnesium is

elevated. Overall, controlling and maintaining magnesium homeostasis represents a helpful intervention to maintain bone integrity (Castiglioni et al., 2013). An increased risk of osteoporotic fractures in individuals who consumed ≥ 4 cups of coffee vs. < 1 cup coffee per day was demonstrated in a study of 31,257 Swedish middle-aged and elderly women (a part of the Swedish Mammography Cohort - SMC) when calcium intake was low ($< 700 \text{ mg}/\text{day}$). However, no higher risks of osteoporosis or fractures were observed in the full SMC with increasing coffee consumption. Calcium intake did not modify the results from the investigations performed in the full SMC or COSM. No association between tea consumption and risk of fractures was found in the studies (Hallström, 2013). Sahmani compare the serum levels of zinc (Zn), copper (Cu) and lipid profile between the postmenopausal women suffering from osteoporosis and the healthy controls. The serum levels of Zn and Cu were similar in both groups ($P > 0.05$). Serum levels of low density lipoprotein (LDL) and total cholesterol (TC) in osteoporosis group was statistically significant when compared to the controls ($P < 0.05$). Correlation analysis showed that there was significant association between body mass index (BMI) and BMD values ($P < 0.05$). There was no correlation between serum Zn, Cu levels with lipid profile ($P > 0.05$). However, they found a negative significant correlation between BMD with LDL ($r = -0.31$, $P = 0.001$) and total cholesterol levels ($r = -0.26$, $P = 0.006$) (Sahmani et al., 2014).

Razmandeh et al. (2014) compared trace elements (Zinc, Copper and Magnesium) concentration in nail, urine and serum among osteoporotic postmenopausal women with control group in Iran. The urine level of trace elements had significant difference between osteoporotic groups and controls ($p < 0.001$). Moreover Mg level significantly differed in serum between two groups ($p < 0.04$). There was no statistically significant difference in trace minerals in nail beyond groups. The Palestinian Osteoporosis Prevention Society conducted a study on the prevalence of osteoporosis among postmenopausal women, they found that around 40% of postmenopausal women were affected (Abd-Alhameed et al., 2010). Trace studies are carried out on osteoporotic patients in Gaza Strip regarding trace minerals levels.

Objectives: Determination of zinc and magnesium levels in osteoporotic patient from Northern Gaza Strip. Verifying the relationship between zinc and magnesium levels in osteoporosis.

Significance Assessment of zinc and magnesium levels in osteoporotic patients; has not be performed in Gaza Strip; hence this study aimed to evaluate levels of these minerals in those patients. This study may indicate a predisposing factors of this common disease in old people.

2. Materials and Methods:

The present study was a case-control study. The study populations were 40 osteoporotic patients aged 40-65 years attending osteoporotic clinics at Al-Shahid Kamal Odwan hospital, Northern Gaza Strip. Controls (40 subjects) were apparently healthy non osteoporotic individuals. **Exclusion criteria:** Osteoporotic patients aged <40 and >65 years and chronic diseases patients are excluded. **Ethical consideration:** An official letter of request sent to the Palestinian Ministry of Health (MOH). The MOH sent a letter to Al-Shahid Kamal Odwan administration to facilitate conduction of the study.

Data collection and biochemical analysis: data collection in this study was through questionnaire interview; patients were asked about their personal, physical, socioeconomical, dietary habits and health status data.

Determination of Magnesium Principle: 5 ml of blood were randomly collected in a plane tube from patients and control groups. Blood samples were collected at Palestinian Medical Relief Society in Gaza. Blood were stored in the freezer at -20 C⁰ until analysis performed. Magnesium in alkaline solution reacts with the chromogenxylydyl Blue to form a purple complex. The presence of glycoetherdiaminotetr acetic acid (GEDTA) that binds calcium ions in the reagent allows the reaction to be specific. Purple color intensity at 520 nm is proportional to the concentration of magnesium in the sample (Thomas, 1998; Chitto et al., 1994).

Determination of Zinc: Principle Zn⁺⁺ reacts with NTR0-PAPS yielding at room temperature a colored complex which intensity is proportional to the zinc concentration preset in the sample. The method does not require sample deproteinization either sample blank (Pasquinelli, 1984; Makino, 1991)

Statistical analysis: The results were analyzed by using SPSS statistical program for determination the significance of the differences between the control and patient groups. T and bi square tests were used to study the differences between means. P value of <0.05 is considered as significant.

3. Results:

The present study included 80 individuals divided into two groups, 40 patients Of osteoporosis aged from 40-60 years and the second group 40 healthy subjects aged from 40-60 years to act as a control group. The results of zinc and magnesium in this study recorded a significant difference between the means of patients and control groups judged by p value of less than <0.05.

Table 1 Levels of Mg and Zn in controls and patients

Items	Cases	Control	t-test	P-value
Zinc mg\dl	73.8±20.3*	83.0±17.3*	2.181	0.032
Mg mg\dl	1.8±0.34*	1.9±0.22*	2.626	0.010

* p value of <0.05 is considered as significant.

There is a significant difference between subjects taking a higher number of eggs and drink more milk per day, versus others whom taking low eggs and milk.

Table 2 Dietary intake of milk and eggs in controls and patients

Items	Cases	Control	t-test	P-value
BMI wt kg/ht m ²	31.0±2.4*	31.2±2.8	0.220	0.827
No of milk/day	0.9±0.9*	0.9±0.6	0.078	0.938
No of eggs/day	1.2±1.2*	1.4±0.8	0.902	0.371

* p value of <0.05 is considered as significant.

Table 3 shows no significant difference between male and female in the studied groups .The percentage of females in this study is higher than male. This result indicated that osteoporosis is more common in females than males.

Table 3 Separation of controls and patients according to gender

	Cases	Control	Chi	P-value
Male	6	3	0.489	0.484
Female	34	37		

The results of groups separation according to the family history of the disease indicated no significant difference between controls and patients groups p>0.05. This result does not indicated a hereditary role in the etiology of Osteoporosis.

Table 4 Separation of controls and patients according to the family history of Osteoporosis

History of disease	Cases	Control	Chi	P-value
Yes	4	1	2.415	0.120

No 36 39

Patients suffering from the disease are exposed to a higher number of fractures, where exposure to break has reached 28%, while controls exposure to break form 27%.

Table 5 Separation of controls and patients according to number of fractures

Fractures	Cases	Control	Chi	P-value
Yes	11	9	0.006	0.938
No	29	31		
%	28%	27%		

Number of subjects taking soft drinks in control and patients are 4, 12 respectively; there is a difference between control and patient groups.

Table 6 Separation of controls and patients according to intake of soft drink

Soft drink	Cases	Control	Chi	P-value
Yes	28	36	1.688	0.194
No	12	4		

There is a significant difference between control and patient groups, judged by p value of less than 0.05. Hormonal therapy may influence and increase the risk of Osteoporosis occurrence.

Table 7 Separation of controls and patients according to hormonal treatment

Hormonal treatment	Cases	Control	Chi	P-value
Yes	28	17	5.622	0.018
No	12	23		

Table 8 separate control and patient s according to the locomotors activity.

A significant difference between control and patient groups $p < 0.05$ is recorded; this result may indicated a role of different activities in preventing people from susceptibility to this disease.

Table 8 Separation of controls and patients according to locomotors activities

Locomotors activity	Cases	Control	Chi	P-value
Yes	5	13	4.649	0.031
No	35	27		

Table 9 shows a difference between control and patients in relation to soft Drinks but this difference is not significant, $p > 0.05$.

Table 9 Separation of controls and patients according to drinking coffee or tea

Coffee or tea	Cases	Control	Chi	P-value
Yes	36	34	0.560	0.454
No	4	6		

4. Discussion:

The present work detected a deficiency of magnesium and zinc levels in osteoporotic patients from Northern Gaza Strip. This result may put the trace minerals and its role in osteoporosis development under the light. The result of the present study is in agreement with the results of Razmandeh et al. (2014), they recorded a deficiency of magnesium and zinc in osteoporotic patients comparing to controls.

Number of females in the present study is higher than males, osteoporosis affects women more than men because they have a smaller bone mass and, once women are post-menopausal, they produce less oestrogen, this finding is in agreement with the results of Castiglioni and others; they reported that women with postmenopausal osteoporosis had significantly higher age, but similar BMI compared to non-osteoporotic controls. Their study shows that level of magnesium is less than normal which is a high risk factor of cardiovascular disease that causes morbidity and mortality (Castiglioni et al., 2013). In a more recent study they compared levels of zinc (Zn), copper (Cu) and lipid profile between the postmenopausal women suffering from osteoporosis and the healthy controls. The study was conducted on 116 postmenopausal women; 58 osteoporosis (age 60.6 ± 3.9 years) and 58 control group (age 55.4 ± 1.7 years). The serum levels of Zn and Cu were measured by atomic absorption spectrophotometry and bone mineral density (BMD) was analyzed by DEXA scan. The serum levels of Zn and Cu were similar in both groups ($P > 0.05$). Serum levels of low density lipoprotein (LDL) and total cholesterol (TC) in osteoporosis group was significantly higher when compared to the controls ($P < 0.05$). Correlation analysis showed that there was significant association between body mass index (BMI) and BMD values ($P < 0.05$). There was no correlation between serum Zn, Cu levels with lipid profile ($P > 0.05$). However, they found a negative significant

correlation between BMD with LDL ($r = -0.31$, $P = 0.001$) and total cholesterol levels ($r = -0.26$, $P = 0.006$) (Sahmani et al., 2014). The present study recorded a relationship between osteoporosis and many risk factors such as daily inactivity, ages, hormonal therapy and coffee drink, the same results were detected by previous studies (Chaconas et al., 2013). Also the present work shows that ages and food that containing zinc and magnesium affect osteoporosis disease, like eggs and milk, that agree with the results of Hyun et al. (2004); they have shown that dietary zinc intake and plasma zinc concentrations were lower in men with osteoporosis at the hip and spine than in men without osteoporosis at those locations. BMDs for the hip, spine, and distal wrist were significantly lower in men in the lowest plasma zinc quartile ($-11.3_{\text{mol/L}}$) than in men with higher plasma zinc concentrations. The association between plasma zinc and BMD was cross-sectional, longitudinal, and independent of age or body mass index. However plasma zinc did not predict bone loss during the 4-y interval.

5. Conclusion:

Zinc and magnesium levels in the serum are significantly lower in postmenopausal women and men with osteoporosis. Hence optimizing levels of those trace minerals in old people may play a protective role from osteoporosis. Controlling of coffee and soft drinks intake, daily exercises and milk and egg intake should be considered. A longitudinal study on osteoporotic patients regarding all trace minerals is recommended.

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مستوى الزنك و الماغنيسيوم في مرضى هشاشة العظام من شمال غزة

كلوات وفتاحية:
هشاشة العظام
الزنك
الماغنيسيوم.

مرض هشاشة العظام يصيب الهيكل العظمي لكبار السن و يتميز بنقصان كتلة و كثافة العظام وخال في استقلاب انسجة العظام مما يزيد من هشاشتها وتعرضها للكسور المتكررة. هدفت هذه الدراسة لتقدير مستوى الزنك و الماغنيسيوم في مرضى هشاشة العظام من شمال قطاع غزة . واشتهلت الدراسة على 40 مريض و40 شخص سليم تتراوح اعمارهم بين 40-65 سنة تم قياس مستويات الزنك و الماغنيسيوم في السيرم في مختبرات جمعية الاغاثة الطبية بغزة باستخدام تقنية قياس الامتصاص الطيفي (دياسست- الهانيا) اظهرت نتائج الدراسة انخفاض طبيعي احصائي في مستويات الزنك و الماغنيسيوم لدى المرضى مقارنة بعينة الضبط وكانت مستويات (الزنك 20.3 ± 73.8 ميلجرام/ديسلتر، 17.3 ± 83.0 ميلجرام/ديسلتر) ، و(الماغنيسيوم 0.34 ± 1.8 ميلجرام/ديسلتر، 0.22 ± 1.9 ميلجرام/ديسلتر) في المرضى و اللاصحاء على التوالي . كذلك اوضحت الدراسة الحالية الدور الايجابي لنوع الجنس والنشاط الرياضي والعلاج الهرموني في هذا المرض بينما لم تظهر دور بعض العوامل المتعلقة بالعادات الغذائية للعينة الودروسة ويتضح من هذه الدراسة الدور الفعال والهم لبعض المعادن النادرة في هذا المرض. نوصي باجراء دراسة اوسع لتشمل العديد من هذه العناصر والتي قد تبرز دورها في التشخيص والحماية من هذا المرض لدى كبار السن.