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EVALUATION OF RISK FACTORS IN PAKISTANI WOMEN WITH VARYING DEGREE OF BONE PAIN

Lubna Naz, Uzma Batool, Nazish Iqbal Khan and Ghazala Yasmeen

Department of Physiology, University of Karachi, Karachi-75270, Pakistan.

ABSTRACT

Bone pain has become a common problem in pre and post menopausal women. This study was conducted in the Department of Physiology, University of Karachi and included only female subjects of age between 36 to 56 years having some kind of bone and joint pain. Subjects were investigated for many pathological and non pathological risk factors for bone pain through a detailed questionnaire. BMI and Waist to hip ratio for the evaluation of obesity were calculated. Blood samples for the estimation of serum alkaline phosphatase and total cholesterol were taken. Several pathological and behavioral risk factors were found in the subjects. Multiple non pathological factors like estrogen deficiency, inadequate dietary calcium and vitamin D intake, physical inactivity, stress and use of caffeine and soft drink were potential risks for bone pain even in the absence of any bone illness. It was observed that majority of the women have many risk factors among them sedentary lifestyle, less exposure to sunlight, obesity, soft drinks use are important. The incidence of bone pain was found to be higher with age. Serum alkaline phosphatase levels were higher in all subjects suggesting some bone disease. There was no significant correlation found between blood Cholestrol and bone pain. Thus it is concluded that incidence of bone pain in Pakistani middle-aged women is an alarming situation. Our lifestyle, diet pattern, physical activity should be modified to avoid the risks for bone pain. Bone pain in old age women is due to lack of protective effects of estrogen therefore during young age some adequate steps regarding lifestyles and diet should be taken to avoid complications later.

Key-words: Risk factors, Pakistani women, bone and joint pain.

INTRODUCTION

Bone pain is a common manifestation of several diseases, like osteomalacia, bone cancer, metastasis from breast cancer, prostate cancer, and so on. It has become a common problem in elderly especially in women after menopause. Estrogen plays a very important role in maintaining normal bone turnover (Pacifici *et al*., 1998). At menopause estrogen deficiency leads to enhanced bone remodeling via accelerated bone resorption thereby decreasing bone mass. There are several pathological and non-pathological risk factors for bone pain. The age-related decrease in bone strength at the hip is largely due to a reduction in bone mineral density (BMD). The pliability of human bone decreases with increasing age, and the incidence of bone fracture increases after about 35 years of age. Estrogen deficiency after menopause accelerates the age-related loss of bone (Ahlborg *et al*., 2001; Riggs *et al*., 1986).Cortical bone loss occurs mainly at the inner (endosteal) surface and partly in the Haversian canals. Cross-sectional studies also indicate that bone size increases with age (Smith *et al*., 1989). Such a change might increase bone strength and compensate, at least in part, for the negative effect of decreases in bone density. Both bone density and bone structure are clinically important, since fractures due to the fragility of bones are independently associated with both low bone mass (Cummings *et al*., 1995). Age relate hip fracture is common in both men and women. The fracture is a stochastic event arising from the interaction between recurrent minor trauma usually from falls and decreased bone strength at the hip (Horsman *et al*., 1985; Grisso *et al*., 1991). In the reduction of bone strength that occurs with age, both low calcium intake and low vitamin D stores have been implicated. The hormone plays an important role in maintaining bone mass in adult women, in part by slowing bone remodeling and in part by maintaining the proper balance between the activity of bone-forming cells (i.e., osteoblasts) and bone-resorbing cells (i.e. osteoclasts). In estrogen-deficient women, osteoclasts are believed to excavate deeper resorption cavities, which osteoblasts are unable to refill completely. This leads to a negative remodeling balance in which there is a small amount of bone lost at every location where bone has undergone remodeling. The combination of increased bone-remodeling units and a negative remodeling balance is the basis for the rapid decrease in bone mass that follows menopause (Turner *et al*., 1994). Excessive bone loss resulting from estrogen deficiency is believed to be the most important of the many factors that determine the overall risk for osteoporosis in women (Richelson *et al*., 1984). Calcium is one of the essential nutrients necessary for healthy bone development. Adequate calcium intake is necessary for the attainment of peak bone mass in the late teens. Vitamin D regulates calcium absorption and excretion, especially when calcium intake is low. There is a statistically significant inverse relationship between consumption of carbonated beverages and bone mineral density in young girls, which places them at increased risk of suffering fractures in the future. Caffeine-containing beverage consumption has been reported to be associated with reduced bone mass and increased fracture risk in some observational studies. Heaney (2002) showed a negative effect of caffeine on the calcium economy. Massey and Wise (1984) showed that a caffeine-induced diuresis

increased urinary calcium loss acutely. The role of caffeine as a risk factor for bone loss is still controversial. Caffeine consumption has been reported to decrease bone mineral density (BMD) (Barrett-Connor *et al*., 1994) increase the risk of hip fracture (Hernandez-Avila *et al*., 1991), and negatively influence calcium retention (Cummings *et al*., 1995; Meyer *et al*., 1997).However, most of the studies reported no overall association between caffeine intake and BMD, fracture rate, or calcium metabolism (Lloyd *et al*., 1997; Hannan *et al*., 2000). Rheumatoid arthritis (RA) is one of the most typical examples of a chronic inflammatory process, which leads to profound changes of the skeleton. In fact, RA and other forms of chronic arthritis are major precipitators of bone loss. Structural skeletal damage plays a major role in the outcome of RA patients since functional disability is a result of accumulating changes of the joint architecture. The pathological role of altered bone turnover in destructive arthritis is strongly supported by the detection of osteoclasts at sites of local bone erosion. These cells are localized at the interphase of inflammatory tissue and bone, and are found in all animal models of destructive arthritis as well as in human RA (Redlich *et al*., 2002; Lubberts *et al*., 2002). GIT disorders are of particular importance because they may be predisposing to the development of bone disease by impairing not only the absorption of dietary factors necessary for the maintenance of healthy bone disease but also their intake and retention.

MATERIALS AND METHODS

The prospective study was conducted in an area of middle average socioeconomic status during the period of March 2009 to November 2009 and included females of age between 36 to 60 years with varying degree of bone pain. The questionnaire was prepared in accordance with the objectives and theme of the study. Subjects were divided into five groups on the basis of their age i.e. group I from 36 to 38 years, group 2 from 39 to 40 years, group 3 from 41 to 45 years, group 4 from 46 to 50 years and group 5 from 51 and above. All participants were asked for previous history of any disease specifically bone disease and fractures. Risk factors for bone pain specifically calcium, vitamin D, caffeine were asked. Use of contraceptives was specifically asked. The body mass index of each subject was calculated by dividing the weight (Kg) of the subject by the square of her height (m) to categorize the underweight and obese females. Laboratory investigations included Blood total Cholesterol and Alkaline phosphatase and were assayed by enzymatic endpoint method using Randox kit.

G1= 36-38 Years (N= 26); G2= 39-40 Years (N= 22); G3= 41-45 Years (N= 27); G4= 46-50 Years (N= 30)
G5= ≥ 51 Years (N= 26)

Table 1. Personal observations..

Variable	36 to 38 years(N=26)	39 to 40 years(N=22)	41 to 45 years(N=27)	46 to 50 years(N=30)	>51years (N=26)
Waist circumference (inches)	34.9 ±5.39	37.2 ±1.98	38.12 ±6.16	40.06 ±3.9	40.45 ±4.54
Hip circumference (inches)	41.36 ±4.05	43.33 ±2.54	43.87 ±4.36	46.2 ±3.68	45.72 ±5.36
W/H ratio	0.84 ±0.05	0.85 ±0.04	0.83 ±0.036	0.86 ±0.028	0.88 ±0.04
Body weight (Kg)	69.36 ±14.44	71.66±10.46	70.81±13.44	78.26±11.87	74.1 ±13.06
Height (cm)	62.18 ±1.99	62.1 ±2.31	61.62 ±1.68	61.4 ±1.5	61.27 ±1
BMI (Kg/m²)	28.03 ±6.74	29.62 ±3.21	29.73 ±5.35	33.15 ±4.51	31.5 ±5.07

BMI= Body mass index; W/H= Waist to Hip ratio; Numerical values are Mean ± SD.

Table 2. Non pathological risk factors for bone pain.

	36 to 38 years(N=26)	39 to 40 years(N=22)	41 to 45 years(N=27)	46 to 50 years(N=30)	≥ 51 years (N=26)
Menopause	0	11.11	6.25	60	98
Calcium Intake	45.45	44.44	56.25	66.66	90.9
Vitamin D intake	20	12	15	10	15
Caffeine Use	98	99	99	96	95
Soft Drinks Use	90.9	98	75	66.66	90.9
Exposure to sunlight	27.27	11.1	50	20	72.72
Physical inactivity	9.09	10	6.25	15	27.27
Exercise	25	17	1	8	2
Stress	81.81	88.88	93.75	97	99

Numerical values are in percentages.

Table 3. Pathologic risk factors.

	36 to 38 years(N=26)	39 to 40 years(N=22)	41 to 45 years(N=27)	46 to 50 years(N=30)	≥ 51 years (N=26)
History of fracture	2	2	6.25	26.66	18.18
Menstrual Irregularities	9.09	22.22	37.5	46.66	2
Renal Insufficiency	54.54	9.09	11.11	18.75	46.66
Anemia	63.63	63.63	33.33	37.5	33.33
GIT Disorders	72.72	18.18	44.44	50	80
Depression	90.9	88.88	75	98	99

Numerical values are in percentages.

Table 4. Subjective and biochemical estimations.

Variable	36 to 38 years(N=26)	39 to 40 years(N=22)	41 to 45 years(N=27)	46 to 50 years (N=30)	≥ 51 years(N=26)
Alkaline Phosphatase (μ/L)	335.16±97.03	339.64 ± 90.94	380.84±115.37	320.78±75.86	429.13±104.75
Cholesterol (mg/dl)	108.97±12.49	105.30 ± 20.36	126.93 ± 30.54	113.87±19.61	121.62±16.80

Numerical values are Mean ± SD

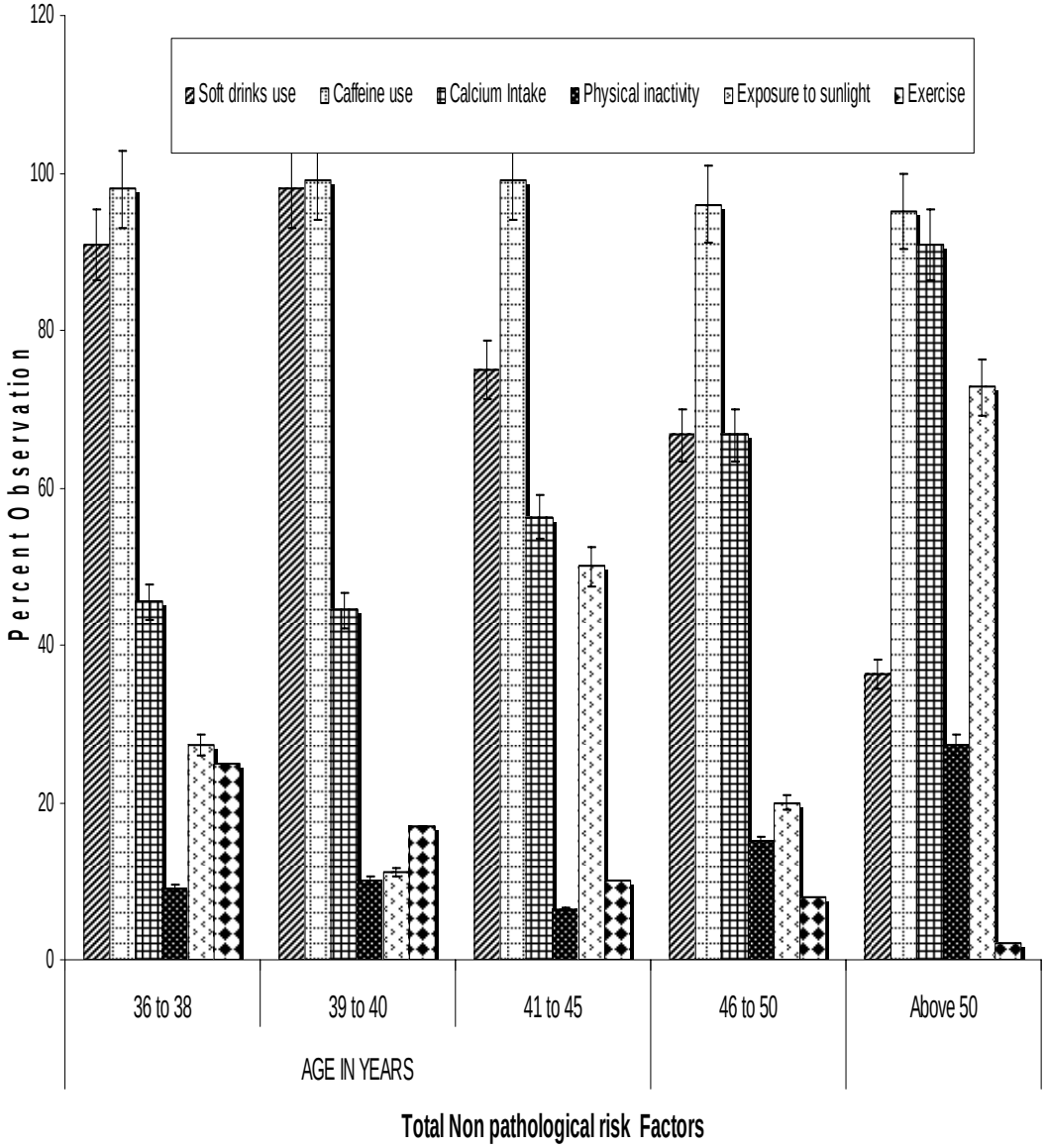

Fig. 1. Total non pathologic risk factors.

RESULTS AND DISCUSSION

Bone pain is an unbearable form of pain specifically in the bone tissue region. It can occur as a result of a wide range of diseases or physical conditions. The obvious, but essential motivation to alleviate bone pain stems from the fact that it is the leading factor in the decrease in quality of life for patients who suffer from it (Lugar *et al*., 2005). Bone pain is a very difficult and diverse problem affecting patients of all ages because it has multiple causes, such as extensive physical stress or diseases such as cancer (Zwas *et al*., 1987; Mantyh *et al*., 2002). A number of mechanisms have been implicated in age-related bone loss at the hip. Perhaps the most common biochemical abnormalities considered to be responsible for bone loss are an increase in secondary hyperparathyroidism and in bone turnover (Riggs *et al*., 1990; Delmas *et al*., 1983).

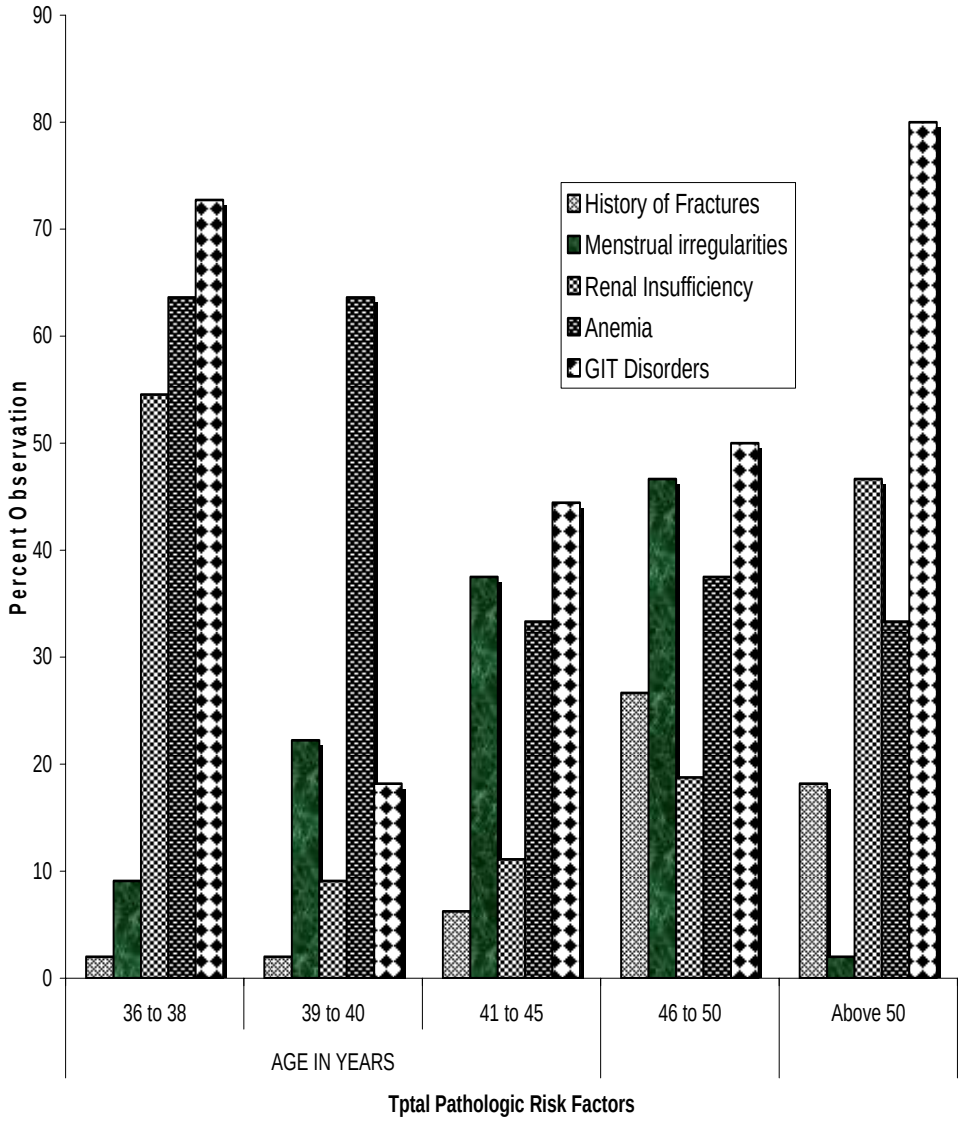

Fig. 2. Total pathologic risk factors.

In women, estrogen deficiency after menopause greatly accelerates bone remodeling and results in a net increase in bone resorption. Even in the years immediately proceeding menopause there can be a drop in estrogen levels that leads to a fall in bone mineral density (Chapurlat *et al*., 2000). As a person ages, body composition changes resulting in losses in bone mass and lean mass and increases in fat mass (Hameed *et al*., 2002). Several studies have examined the relative contribution of fat mass and lean body mass to BMD in the aging population (Ravaglia *et al*., 2000; Taaffe *et al*., 2001). The BMI was found to be higher in all age groups except older groups may be due to age related loss of body tissues (Table 1). Waist to hip ratio was also higher in all groups (Table I). A Scottish survey of 858 people aged 58 demonstrated a high prevalence of pain affecting the knees, hips, hands, neck and back (Adamson *et al*., 2006) the frequency of hip and knee pain was twice as high in obese respondents. Obesity is a strong risk factor for bone pain and was noted in almost all subjects. Obesity has been linked with physical disability (Odding *et al*., 1998; Thomas *et al*., 2008). The prevalence of non pathological risk factors was also found to be higher in our study (Fig. 1). In the reduction of bone strength that occurs with age, both low calcium intake (Dawson-Hughes *et al*., 1991) and low vitamin D stores (Peacock and Hordon, 1989) have been implicated. Dietary intake of calcium decreases with age (Alaimo *et al*., 1994), and a substantial proportion of the elderly take less than

the Recommended Dietary Allowance of 800 mg. There is also an age-related reduction in vitamin D status, a major determinant of calcium absorption (Baker *et al*., 1980). Calcium intake was different in all age groups. 45.45% subjects of group I take calcium indifferent forms like milk, dairy products and supplements etc. in group II only 44.44% subjects reported calcium ingestion whereas 56.25% subjects of group III showed this intake. Intake of calcium is relatively higher in older age groups i.e. 66.66% subjects of group IV and 90.9% subjects in group V dietary intake of calcium (Table 2; Fig. 1). This increase intake in older age groups may be due to impaired digestive ability at old age and people prefer milk over heavy meals.

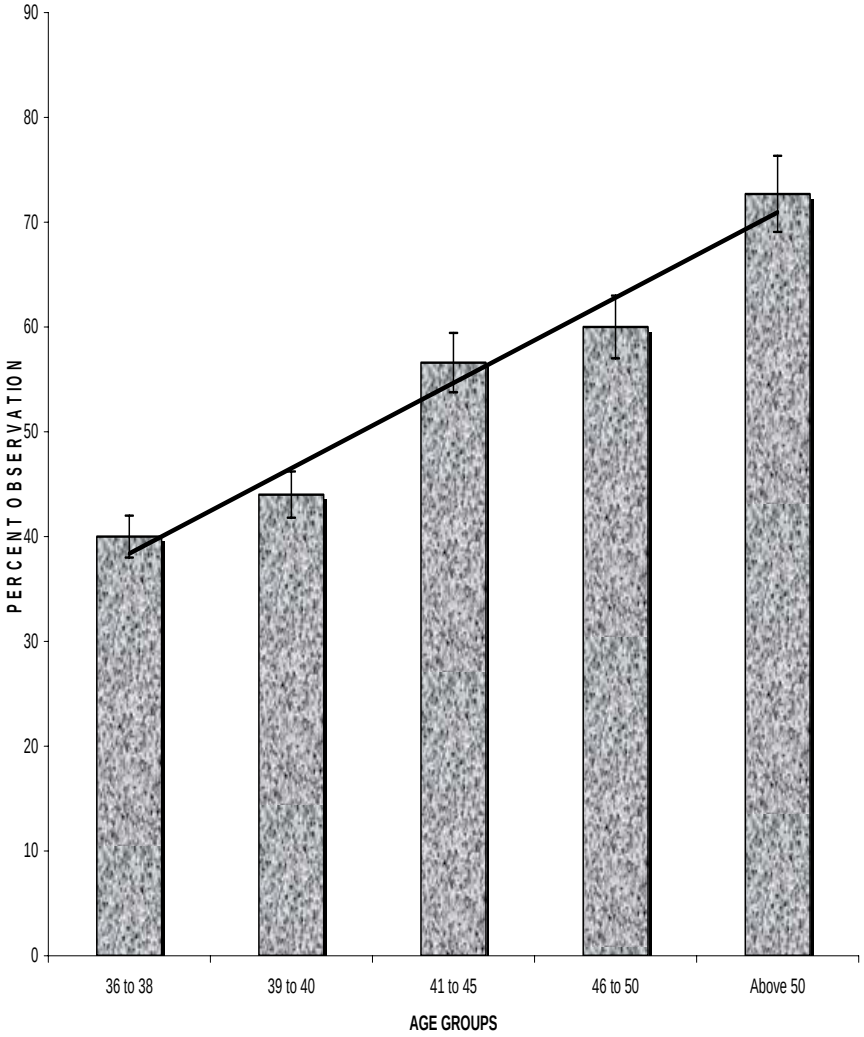

Fig. 3. Incidence of bone pain in various age groups.

Several epidemiological studies have reported the influence of caffeine on osteoporosis, but the effects of coffee on bone metabolism remain controversial (Lloyd *et al*., 1997; Stein *et al*., 1996). Use of caffeine was demonstrated by above 90% subjects in all the five age groups (Table 2; Fig. 1)Caffeine has a variety of pharmacological actions and cellular responses in bone metabolism, resulting in increased urinary calcium excretion and in vitro inhibition on the proliferation of osteoblast-like cells (Johnell *et al*., 1995).After caffeine , use of soft drinks was identified in around 90% in the groups I, II &V whereas relatively less number of subjects i.e., 65 to 75 % subjects in group III & IV take soft drinks routinely (Table 2; Fig. 1).There has been a hypothesis that the phosphoric acid contained in some soft drinks (colas) displaces calcium from the bones, lowering bone density of the skeleton and leading to conditions such as osteoporosis and very weak bones. There is a statistically significant inverse relationship between consumption of carbonated beverages and bone mineral density in young girls, which places them at increased risk of suffering fractures in the future. The body's main source of vitamin D arises from the manufacture of this vitamin in the skin on exposure to sunlight. As our study included female subjects only and in our culture most females are

house hold and that is why they normally do not expose to sun light which serves as a risk factor for bone pain. Only less than 30 % subjects in group I to IV routinely exposed to sunlight regularly whereas over 70% in group V were exposed to sunlight on daily basis (Table 2; Fig. 1). Exercise helps keep the joints flexible, the muscles around the joints strong, bone, and cartilage tissue strong and healthy; and reduces pain. Exercise can help slow the progress of osteoporosis and build strong bone Women relatively in older age group showed more physical inactivity and almost absence of any kind of exercise whereas comparatively young ones exhibited more activity and at least some exercise pattern but not on daily basis (Table 2; Fig. 1) Stress has been a common feature of our population in current situation and above 80% subjects in our study including all age groups reflected the same picture. It was present over 80% in all age groups and there was a direct relationship between age and stress (Table 2; Fig. 1). The fracture is a stochastic event arising from the interaction between recurrent minor trauma usually from falls and decreased bone strength at the hip (Horsman *et al*., 1985; Grisso *et al*., 1991). Similar results were found in our study and fracture was reported in older age group more than young ones (Table 3; Fig. 2). Abnormal absence of menstrual periods (amenorrhea) and low estrogen level (menopause) can bring on osteoporosis. There was a consistent increase in menstrual irregularities found with advancing age especially prior to menopause. Group V did not exhibit any indication because of menopause (Table 3).Variable degrees of renal problems were found in our study. Incidence was high in minimum and maximum age groups may be due to sexual trauma in young females and age related atrophy in older ones but these are minor reasons (Table 3).Anemia or iron deficiency was found in group I & II mainly because of more loss during menstruation and during pregnancy (Table 3).GIT disorders are responsible for impaired calcium absorption and eventually affect bones. These problems were found mainly in group I &V but other did not show any significant results (Table 3).

The high predominance of women with depressive disorders was explained in many studies. The findings of Freeman (Freeman *et al*., 2004; 2006) with regard to estrogen showed that both high and low estrogen were associated with depression. More recently, their data suggest that variability in estrogen levels may drive depression, that is, those women who show rapid changes from high to low estrogen and vice versa are those who develop depressive symptoms during the perimenopause transition. Incidence of depression was very high in all age groups especially in pre and post menopausal women (Table 3). Alkaline phosphatase is an enzyme found in all body tissues, with the highest concentrations found in growing bones. Alkaline phosphatase plays a role in the calcification of cartilage and bone and catalyzes the hydrolysis of the phosphoric acid ester by causing a supersaturation of phosphate ions. It is also believed that alkaline phosphatase also plays a role in bone resorption by removing a layer of phosphate that is present on the surface of bones. High levels of alkaline phosphatase in the blood can indicate diseases of the bones, liver, bile system or malignancies. In women especially postmenopausal women the increase of this bone formation marker in life may be an expression of increased bone turnover, which is partially the cause of osteoporosis (Lumachi *et al*., 2009). Alkaline phosphatase levels were found to be very high in all age groups. (Table 4). Cholestrol levels were found in normal limits (Table 4).

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