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Correlation between postmenopausal period and certain hepatic enzymes in women of tertiary hospitals of Punjab

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Abstract
At the time of menopause female sexual cycle ceases and female sex hormones diminish rapidly. It is characterized by various physiological, psychological and biochemical changes, and also metabolic bone disorders. Therefore in the present study we analyzed the level of aspartate aminotransferase, alanine aminotransferase, serum proteins, along with calcium and phosphorus levels in premenopausal women (n=40) and postmenopausal women (n=40). In premenopausal women the concentration of aspartate aminotransferase was elevated significantly as compared to postmenopausal women ($p<0.001$) but, the concentration of alanine aminotransferase was increased non significantly. The concentration of total serum protein increases in post menopausal women non significantly as compared to pre menopausal women's whereas, the albumin level was decreased significantly in post menopausal women ($p<0.0001$). The serum calcium level was declined significantly in post menopausal women as compared to pre menopausal women's ($p<0.0001$). Thus our study demonstrated that, as age advances liver gets irritated and the liver functions gets disturbed. The decreased concentration of calcium in postmenopausal women indicates that they are more prone to fractures and osteoporosis.

Keywords menopause, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), osteoporosis

1. Introduction

Menopause, a period during which the female sexual cycle ceases and female sex hormones diminish rapidly. It occurs between 45-55 years of age. It is characterized by hot flushes, night sweats and various other psychological and biochemical changes occur [1]. It also leads to metabolic bone disorders. Bone metabolism is a dynamic and continuous process to maintain a balance between the resorption of old and injured bone initiated by osteoclasts and the formation of new bone under the control of osteoblasts. In general, the processes of bone formation and resorption are 'coupled', so that there is no net change in the bone mass [2]. With the onset of menopause, rapid bone loss occurs, which is believed to average approximately 2% to 3% over the following 5 to 10 yrs, being greatest in the early postmenopausal years. Life time losses may reach 30% to 40% of the peak bone mass in women may lead to osteoporosis [3-5].

Osteoporosis is a major health and economic problem, characterized by low bone mass and microarchitect deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. This silently progressing metabolic bone disease is widely prevalent in India and osteoporotic fractures are a common cause of morbidity and mortality in adult Indian men and women. Age is an important factor contributing to the increased development of osteoporosis. According to National Health and Nutrition Examination Survey (NHANES III), an estimated 14 million American women over age 50 years are affected by low bone density at the hip. The prevalence of osteoporosis increases with age for all sites, and by WHO definition up to 70% of women over the age 80 years have osteoporosis [6, 7].

The occurrence of Osteoporosis in postmenopausal women is very common problem especially in India who are exposed to many of the risk factors like Family history of osteoporosis, history of anorexia or bulimia, prolonged amenorrhea, low calcium diet, lack of exercise, Vitamin D deficiency.

The liver is a major organ of the body that performs diverse functions, essential for life. Onset of menopause also alters the liver functions. The most common liver function tests include alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin and albumin are effective modalities to detect hepatic dysfunction. Aspartate aminotransferase (AST) formerly called serum glutamic- oxaloacetic transaminase (SGOT) enzyme is necessary for energy production. This enzyme reflects damage to the hepatic cell. It may be elevated in other conditions such as myocardial infarction. Although AST is not a specific for liver as the ALT. ALT and AST are useful in assessing the etiology of liver enzyme abnormalities. AST is elevated in liver and heart disease. ALT, formerly called serum glutamate pyruvate transaminase or SGPT, is another enzyme necessary for energy production. ALT, produced by the liver, abnormally increased in conditions, where cells of the liver have been inflamed or undergone cell death. As the cells are damaged, the ALT leaks into the bloodstream leading to a rise in the serum levels. Any form of hepatic cell damage can result in an elevation in the ALT. It is

the most sensitive marker for liver cell damage [8, 9]. Calcium, a component of skeleton, soft tissues, and extra cellular fluid is the fifth most common element and the most prevalent cation found in the body. The skeleton contains 99% of the body's calcium. Soft tissues and extra cellular fluid contain about1% of the body's calcium. Of the protein bound calcium fraction, approximately 80% is associated with albumin and 20% with globulins [1, 10, 11]. So, because of these backgrounds, present study was carried out to assess the clinical utility of biochemical markers of bone turnover like Calcium and Alkaline Phosphatase along with hepatic enzymes such as ALT, AST in premenopausal women and post menopausal women in the tertiary care hospitals of Punjab.

2. Material and methods

The present case-control study was carried out in the Department of Biochemistry, Government Medical College - Patiala in collaboration with Department of Obstetrics and Gynaecology, Rajindra Hospital Patiala on 80 subjects in the age range of 25 - 70 years. These subjects were taken from general population attending the outdoor patients of Department of Obstetrics and Gynaecology Rajindra Hospital Patiala and were divided into following two groups based on their menopausal status.

- **Group- 1:** 40 premenopausal women with age range of 25 - 45 years
- **Group-2:** 40 postmenopausal women in the age range of 50 - 70 years.

These subjects were recruited from rural and as well as from urban areas of Patiala District of Punjab state.

Ethical Issues

The study protocol was approved by the institutional ethic committee. Study details & potential risks and benefits were explained to individuals taking part in the study and at least one attendant. A written informed consent was obtained voluntarily from the subjects before entering into the study.

Inclusion Criteria

- Premenopausal women in the age group of 25-45 years
- Postmenopausal women in the age group of 50-70 years with natural menopause

All subjects recruited for the study were vegetarian and there was no positive family history of CVD, thyroid dysfunction, Diabetes, Kidney disease etc, in these subjects. These subjects were interviewed by questionnaire regarding the detailed information on their lifestyle, medical history, diet etc.

Exclusion Criteria

- Age less than 25 years and more than 70 years
- Pregnancy
- Abnormal uterine bleeding
- Surgical menopause
- Hypertension, Diabetes Mellitus, Thyroid disorders
- Hepatic disease
- Acute illness
- Patients on lipid lowering medication, patients on HRT.

Measurements of Anthropometric Parameters

The examination of body weight was done by taking weight in kilogram (kg) and height was measured in centimeters. The BMI was calculated from the formula: BMI = weight in kg/(height in meters squared). A complete lipid profile, fasting and postprandial glucose levels, and Blood pressure (systolic and diasystolic) were carried out in adolescents, who entered the study as per a predesigned performa for assessing the signs of chronic heart failure, diabetes and also the presence of any exclusion criteria.

Collection and processing of blood sample

Fasting (12 hours fasting) blood sample (approximately 5 ml) were collected plain vacutainer from both the groups (Premenopausal and Postmenopausal women subjects) and Plain vacutainer was kept at 37 °C for 20 min and then centrifuged at 3000rpm for 15 minutes. A clear supernatant (serum) was used for the estimation of various biochemical assays.

Biochemical Assays

1) **Determination of S.G.O.T (AST)**: SGOT levels in the serum of postmenopausal and premenopausal women were determined by using commercial available standarized kits manufactured by Agappe Diagnostics Limited, Mumbai (India)based on the principle of Moss and Henderson in 1999, kinetic IFCC method [12].
2) **Determination of S.G.P.T(ALT)**: SGPT levels in the serum of postmenopausal and premenopausal women were determined by using commercial available standarized kits manufactured by Accurex Biomedical Private Limited, Mumbai (India) [13].
3) **Determination of Alkaline Phosphatase (ALP)**: ALP levels in the serum of postmenopausal and premenopausal women were determined by using commercial available standardized kit manufactured by Transasia Biomedical Private Limited, Mumbai (India) based on the principle of Bessey, 1946 [14].
4) **Determination of calcium:** Calcium levels in the serum of postmenopausal and premenopausal women were determined by using commercial available standardized kit manufactured by Transasia Biomedical Private Limited, Mumbai (India) based on the OCPC (O–Cresophthalein Complexone) method by Tietz,1947 [15]

3. Statistical Analysis

The data was expressed as Mean ± SD and analyzed with the SPSS 16.0.7 statistical software package. Differences between the premenopausal and post menopausal women were evaluated using the Student's independent samples "t" test. Differences were considered statistically significant at $p < 0.05$.

4. Results and discussion

ALT and AST markers of hepatic injury enzymes was significantly ($p \leq 0.05$) increased by 19.65% (from 35.62± 5.01 to 42.62± 4.22 IU/ml) and 18.06% (from 38.75± 8.09 to 45.75± 9.41 IU/ml respectively (Table - 1) in post menopausal women

in the present study in comparison to pre menopausal women's. AST and ALT are necessary enzymes for the production of energy. These enzymes reflect damage to the hepatic cell. It may be elevated in other conditions such as myocardial infarction. Although AST is not a specific for liver as the ALT. ALT and AST are useful in assessing the etiology of liver enzyme abnormalities. ALT, produced by the liver, abnormally increased in conditions, where cells of the liver have been inflamed or undergone cell death. As the cells are damaged, the ALT leaks into the bloodstream leading to a rise in the serum levels. Any form of hepatic cell damage can result in an elevation in the ALT. It is the most sensitive marker for liver cell damage [8, 9].

ALP, a ubiquitous enzyme was significantly ($p \leq 0.01$) increased by 24.52% (from 86.85± 7.36 to107.9± 6.88 IU/ml) that plays an important role in osteoid formation and bone mineralization (Table-1). The serum ALP pool consists of several dimeric isoforms that originate from various tissues, such as the liver, bone, intestine, spleen, kidney and placenta [18-21]. In adults with normal liver function, approximately 50% of the total ALP activity in serum is derived from the liver, whereas 50% arises from bone. A significant increase in AST, ALT and ALP in the present study suggested that postmenopausal women are prone to liver disease/ bone disease and /or undergone cell death. Calcium, a component of skeleton, soft tissues, and extra cellular fluid is the fifth most common element and the most prevalent cation found in the body. The skeleton contains 99% of the body's calcium. Soft tissues and extra cellular fluid contain about1% of the body's calcium. Of the protein bound calcium fraction, approximately 80% is associated with albumin and 20% with globulins. Bone mineralization and rate of bone turnover are controlled by a number of hormones in the human body. Parathyroid hormone causes bone resorption and helps to maintain blood calcium levels. Estrogens exert a major effect in women on bone remodeling by inhibiting interleukin. Production that reduces bone resorption and also controls the timing of osteoclasts apoptosis. Bone turnover increases to high levels in women soon after menopause. In addition, estrogens deficiency may induce calcium loss by indirect effects on extra skeletal calcium homeostasis [22-24]. A significant ($p \leq 0.05$) decrease in calcium levels in postmenopausal women was recorded in the present study (Table-1) suggested the initiation of osteoporosis in postmenopausal women.

Table 1: Changes in serum AST, ALT and ALP levels of premenopausal and Postmenopausal women of tertiary care hospitals of Punjab.

Biochemical Assays	Premenopausal Women	Premenopausal Women
AST (IU/ml)	35.62± 5.01	42.62± 4.22 (+ 19.65)*
(ALT (IU/ml)	38.75± 8.09	45.75± 9.41 (+ 18.06)*
ALP (IU/ml)	86.85± 7.36	107.90± 6.88 (+ 24.52)**
Calcium (mg/dL)	7.465± 0.811	5.985± 1.103 (-19.38)*

[a]Values are expressed as Mean ± S.D of 40 observations

[b]Values in parentheses represent percentage changes compared to normal healthy non smokers

* $P \leq 0.05$, ** $P \leq 0.01$

5. Conclusion

The aforementioned observations suggested that postmenopausal women in Punjab (India) are more prone to liver damage and exhibit altered liver function, as the age advances. The decreased concentration of calcium and increased levels of ALP in postmenopausal women indicates that they are more prone to fractures & osteoporosis and warrants further investigations with large clinical trials.

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