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# Blood Lead Level and Δ-Aminolevulinic Acid Dehydratase Activity in Pre-Menopausal and Postmenopausal Women

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**Abstract:** To describe the relationship of blood lead levels (BLL) and blood, δ-aminolevulinic acid dehydratase (ALAD) activity and haematocrit value (Hct) to menopause , were examined 17 pre-or perimenopausal (PreM) and 17 postmenopausal women (PosM) from Prishtina City, the capital of Republic Kosovo. The mean age of the PreM women was 28.8 years (21-46), with a mean blood lead level of 1.2 µg/dL (SD=0.583 µg/dL ) , the mean blood ALAD activity 53.2 U/LE (SD= 2.8 U/LE) and haematocrit value 42.1 % (SD= 4.3 %). The mean age of the PosM women was 53.6 years (43-67), with a mean blood lead level 1.9 µg/dL (SD=0.94 µg/dL), the mean blood ALAD activity 44.4 U/LE (SD=7.2 U/LE) and haematocrit value 42.1 % ( SD= 4.3 %) and 42.2 % (SD=4.4 %). The BPb level of PosM women was significantly higher (P<0.001) in comparison with the BPb level in PreM women. The blood ALAD activity of PosM was significantly inhibited (P<0.002) in comparison with blood ALAD activity in PreM women. The haematocrit values were relatively unchanged. There was established significantly negative correlation between BPb and blood ALAD activity (r=- 0.605; P<0.01) in the PreM women. These results support the hypothesis that release of bone lead stores increases during menopause and constitutes an internal source of exposure possibly associated with adverse health effects on women in menopause transition.

**Keywords:** Women, menopause, blood, ALAD, Hct, lead

## INTRODUCTION

For decades the population of Prishtina (the capital of The Republic of Kosovo), were exposed to high environmental lead levels because of combustion of leaded gasoline and poor environmental control of industrial activities. Despite reductions in the environmental lead exposure, lead poisoning remains a significant public health problem [1]. While young children and some adults continue to be at risk from exogenous sources of lead exposure, new evidence suggests that some person's may be at risk for recurring exposure to lead previously accumulated over time in the skeleton [2, 3].Most (95 %) of lead to which adults are exposed is sequestered in bone, with remainder deposited in blood and other soft tissues. Lead in blood has a short half-life (30 days), whereas lead in bone has a half-life of up to 25 years [4]. Mineral absorption and resorption are affected by many factors, including age, diet, weight-bearing, activity, trauma, metabolic disorders,

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hormonal status, pregnancy, lactation, and menopause [5, 6, 7, 8, 9].Recently, pregnant and lactating women and those undergoing menopause have been identified as additional groups in the population who may be at risk for increased blood levels because of potential lead mobilization during conditions of high bone turnover [10]. The magnitude of lead mobilization from bone and this significance for overall lead exposure in menopausal women has not been empirically measured. It has been estimated that trabecular bone loss is approximately 6-2percent per year during the first 3to 4years after menopause [11], after that it decreases for 8-5years and finally levels off at less than 1percent per year. In response to these factors, both lead and calcium are deposited in the skeleton and may act similarly [12, 13, 14] Lead competes with calcium for transporting and binding sites, and when calcium is released from bone, lead is also released [15, 16, 17]. Additionally, lead does not accumulate uniformly throughout the skeleton but it is selectively taken up at different types of bone (e.g. trabecular bone more than cortical bone); [18, 19, 20, 21]. These events may be of particular importance to women of changing dynamics of bone mineral metabolism related to events such as pregnancy, lactation, and menopause[22, 23]. Over her life time, a women loses up to 50percent of trabecular bone and 30 percent of cortical bone , and 30to 50percent of this bone loss occurs in the early postmenopausal years [24, 25]. Increases in blood lead associated with menopause are of concern because recent research has linked lead in the blood, at levels previously thought to be safe, to a number of adverse health outcomes in adults, including increased blood pressure, [26, 27] reduced kidney function [28] and increased risk of atherosclerosis and cardiovascular disease mortality [29]. Obviously, the effects of lead exposure in postmenopausal women are a highly neglected research area, with needs of considerable focus in the future. It is essential to identify a risk groups in population to ensure reliable risk assessment and cost-effective risk reduction. Delta aminolevulinic acid dehydratase (ALAD) activity in erythrocytes is considered the most sensitive indicator of Pb exposure [30, 31]. On the other hand, Hernberg and Nikkanen (1970) suggested that erythrocyte ALAD activity is more accurate and more sensitive than aminolevulinic acid (ALA) in urine as an indicator of the amount of circulating lead. The objective of this study was to examine the relationship between blood lead and ALAD activity, and haemtocrit value in pre-menopausal and postmenopausal women from Prishtina city.

## MATERIALS AND METHODS

*Sample collection*

Blood samples were obtained by venipuncture from all women during medical examination in Gynaecological and Obstetric Clinic “FATI IM” in Prishtina city. Blood lead level was measured by Graphite Furnance Atomic Absorbtion Spectrophotometry GFAAS), at laboratory of National Institute of Public Health (Prishtina, Kosovo). This laboratory is approved for lead analysis by Center for Desease Control and Prevention (Atlanta, Georgia. U.S.A.), beause of its rigorous quality control procedures. The assay detection limit was 1µg/dl .

*Blood ALA-D activity*

Blood ALAD activity was measured according to the CEC Standardized method [32]. The haematocrit was determined in heparynized capillary tubes, centrifuged for 8minutes at 10.000rpm (Haemofuge Heraues).

*Menopausal status*

A variable was created to categorize women as premenopausal (ovarian function intact), surgically menopasusal (both ovaries removed surgically before cessation of menses), or naturally menopausal (no surgical loss of ovarian function). Participants without a history of reproductive surgery were classified as premenopausal if they reported having had a menstrual period during the previous 12months and postmenopausal if they did not , consistent with World Health Organization criteria .

*Statistical analysis*

Statistical analysis of the results was carried out with Sigma stat 32programs ( 2004STAT Software). For each continuous variable, a distribution form was determined, and significant differences between means were checked by Student's t test .

The table 1summarizes the blood lead level (BPb), delta-aminolevulinic acid dehydratase (ALAD) activity and haematocrit value obtained on pre-or perimenopasusal (PreM) and postmenopausal ( PosM) women. The BLL in the PosM women was significantly higher ($P<0.001$) in comparison with BLL in the PreM women.The blood ALA-D activity of postmenopausal women was significantly inhibited in comparison with ALA-D activity in the blood of pre-menopausal women.

Table 1. Blood lead level (BLL), δ-aminolevulinic acid dehydratase (ALAD) activity, and haematocrit (Hct) value in pre-menopausal (PreM) and postmenopausal (PosM) women.

| Parameters | N | Pre-menopausal Women | Postmenopausal Women |
|---|---|---|---|
| Age/ years | 17 | 28.8 (21-46) | 53.5 (43-67) |
| BLL µg/dL** | 17 | 1.23±0.58 | 1.90±0.94 |
| ALAD (U/LE** | 17 | 53.2±2.8 | 44.4±7.2 |
| Hct (%) | 17 | 42.1±4.3 | 42.2±4.4 |

Note: Values are expressed as means ± SD= Standard deviation. N=number of subjects. ** $P < 0.001$.

## DISCUSSION

The higher concentration of BPb established in PosM women is in accordance with results of several authors [33, 34, 35], who also recorded the higher BPb in the postmenopausal women. Our results of higher BPb level in PosM women are also in accordance with results of Sun and co-workers [36], who in Chinese population found dose-response relationship between lead exposure and prevalence of osteoporosis. Smith and co-workers [37], using endogenous stable lead isotopes as a tracer of skeletal lead release in environmentally exposed subjects ( 6-1 µg/dL blood level) indicated that skeleton contributed from 70-40% of the lead in the blood. This suggests that blood lead levels not only reflect recent exogenous exposure, but that under steady-state conditions they also reflect the release of older accumulated lead from skeleton. Complementary observations were reported by [2, 13] who found that postmenopausal women had significantly higher blood lead levels than pre-menopausal women, even after controlling for age, race, income, alcohol

consumption, and other variables. Our results of significant inhibition of ALAD activity recorded in the blood of PosM women are in accordance with results of Murata and co-workers [38] who during estimation of critical dose of the association between the blood lead concentration (BPb) and δ – aminolevulinic acid (ALA) levels in plasma (ALA-P) blood, and urine (ALA-U), and the activity of δ-aminolevulinic acid dehydratase (ALAD), in 186 Japanese lead workers, aged 69-18years, with BPb levels of 2.1- 62.9µg/dL found that ALA – related parameters were significantly correlated with BLL. The benchmark dose (BMDs), computed from the 186workers, after controlling for age, were 20.9-15.3 µg /dL for ALA levels, and 2.7µg/dL for ALAD activity. In conclusion, the inhibition of ALAD activity to lead low levels of less than ( 1.2and 1.9 µg/dL in PreM and PosM women respectively), 10 µg/dL is suggested to cause immediately increased levels of ALA-P and ALA-B. Although such subtle changes in ALA at low levels of exposure may hardly lead to direct neuropsychological dysfunction or disability in postmenopausal women. The inhibition of ALAD due to lead at low levels of less than 10 µg/dl is suggested to cause immediately increased levels of ALA-P and ALA-B. Although such suitable changes in ALA at low levels of exposure may hardly lead to direct impairment or disability in human life [39]. To our knowledge, this study is the first to have examined the relation between blood lead levels and ALA-D activity in pre – menopausal and postmenopausal women .

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