

## Assessment of serum prolactin, prothrombin time and activated partial thromboplastin time in post-menopausal women

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### Abstract

Post-menopause is described as the period following twelve consecutive months no menstruation, indicating the end of the reproductive phase and ovarian failure, followed by a reduction in estrogen and several physical and psychological changes. This study aimed to determine the serum prolactin and some hematological values in post-menopausal women. Blood samples were drawn in 70 women (aged 53-80 years) who have not menstruated for more than 12 consecutive months and 30 control subjects who were apparently healthy aged 20-47 years. These women attained natural menopause and were not taken any hormonal intervention. Post-menopausal women had significantly lower prolactin levels ( $12.121 \pm 4.991$  ng/ml) compared to apparently healthy women ( $21.916 \pm 12.416$  ng/ml;  $p < 0.001$ ). The mean value of activated partial thromboplastin time (APTT) significantly increased ( $34.388 \pm 2.751$  second)) compared to control subjects ( $31.296 \pm 3.291$  second;  $p = 0.044$ ). There were significant lower levels of prolactin and higher levels of activated partial thromboplastin time in post-menopausal women.

**Keywords:** Prolactin; Post-menopausal; Women; Prothrombin time; Thromboplastin

### 1. Introduction

The World Health Organization defines menopause as the total cessation of menstruation in a woman for 1 year or more. Menopause occurs basically from the decrease in estradiol due to absent of ovarian follicular activity. Globally, there is variation in the age and symptoms of menopause. The biological make up (genetics) and reproductive history (environmental and behavioral factors) had been reported to be responsible for such variation in different parts of the world. The mean and median ages of Nigeria women at menopause were 48.4 and 48.0 years (Okonofua *et al.*, 1990; Ozumba *et al.*, 2004; Kadam *et al.*, 2018). Prolactin is vital in normal mammary gland growth and development, along with lactation. Both animal and *in vitro* studies have reported prolactin involvement in tumorigenesis by advancing cell proliferation, raising cell motility, and boosting tumor vascularization (Clevenger *et al.*, 2003; Liby *et al.*, 2003). Prolactin and its receptor are present in normal and malignant tissues, but its concentrations are mostly increased in malignant tissue (Reynolds *et al.*, 1997; Gill *et al.*, 2001). In elderly women, prothrombin time (PT) and activated partial thromboplastin time levels are likely to be moderately increased than in younger adults, with studies showing a positive association between aging and extended clotting times. However, standard healthy adult prothrombin time is 11-13.5 seconds and activated partial thromboplastin time is 25-35 seconds, elderly women may have moderately increased results (Nakae *et al.*, 2020). Though, some data indicated increased prolactin, PT & APTT in elderly, while others reported that gender differences might be less significant than age-related increases, especially in postmenopausal women (Kamal *et al.*, 2007; Nakae *et al.*, 2020). This case-control study was conducted to determine the level of prolactin, PT, aPTT & erythrocyte sedimentation rate in postmenopausal women.

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## 2. Materials and Methods

This case-control study was conducted at the laboratory of Enugu State University Teaching Hospital (ESUTH) from September 2024 to August 2025. The study was approved by the ethical committee of the Enugu State University Teaching Hospital, and the participants were fully informed about the research before participation.

### 2.1. Inclusion and exclusion criteria

Women who had stopped menstruation without any hormonal or surgical intervention were enrolled. Apparently healthy women who were having regular menstruation were included as control subjects. The age of the controls was 20–47 years. Women with lifestyle habits such as tobacco and smoking, surgically induced menopause or history of coagulopathies, and also medications known to affect the haematological and hormonal values were excluded from the study.

### 2.2. Blood sample collection

Blood were drawn from the subjects. Two milliliters of the venous blood were dispensed into Ethylene diamine tetra-acetic acid (EDTA) containers to determine erythrocyte sedimentation rate (ESR). Nine milliliters of the blood was also dispensed into 0.33mL of 3.2% tri-sodium citrate to determine PT and aPTT. Again, 2mL of the blood was emptied into a plain tube, allowed to clot and separated to obtain serum used for prolactin level assay by Enzyme Linked Immunosorbent Assay technique.

### 2.3. Sample analysis

#### 2.3.1. Prolactin assay

Sample: Non-hemolysed, non-lipaemic, freshly drawn serum samples were used. Serum samples not assayed immediately were arranged in small aliquots, stored and frozen appropriately.

Procedure: Serum prolactin is measured using a non-competitive (Sandwich) ELISA with a micro-well strip reader. The color intensity produced from the reaction is directly proportional to the amount of prolactin present (Prolactin, 1995).

#### 2.3.2. Prothrombin time (PT) test

A 9ml of venous blood was collected into a plastic tube containing 1ml of aqueous tri-sodium citrate anticoagulant. The blood was centrifuged at 1200g for 15 minutes to obtain platelet poor plasma. Thromboplastin reagent (0.25ml) was delivered into a small glass tube and placed in a 37°C water bath for two minutes. Fifty microliter of plasma was added, mixed, stop-watch was started immediately with tilting of the tube in water bath and examine for the clot formation. At first sign of clot formation, stop watch was stopped and result was reported in seconds (Cheesbrough, 2006).

#### 2.3.3. Activated partial thromboplastin time (APTT) test

Kaolin/platelet substitute (0.2ml) was well-mixed and delivered into a small glass tube. Plasma (0.1ml) was mixed, added into the same tube and incubated at 37°C for 2 minutes. 0.1ml 0.025mol/l calcium chloride was mixed and added, stop-watch was started immediately with tilting of the tube in water bath and examine for the clot formation (Cheesbrough, 2006).

### 2.4. Statistical Analysis

Statistical Package for Social Sciences version 25 was used to perform the statistical analyses. The data were expressed as mean±SD. The mean values were tested for significance using an independent T-test. Pearson's correlation coefficients were used to determine the relationship between PT, APTT, prolactin and age. Value of  $p < 0.05$  was accepted as statistically significant.

## 3. Results

Table 1 compares prolactin, PT, APTT and ESR between postmenopausal women and control subjects. The mean prolactin ( $12.12 \pm 4.99$  ng/ml) of postmenopausal women were significantly lower compared with control subjects ( $21.92 \pm 12.42$  ng/ml;  $p < 0.001$ ). The mean APTT ( $34.39 \pm 2.75$ ) of postmenopausal women were significantly higher compared with control subjects ( $31.29 \pm 3.29$  second;  $p = 0.044$ ) (Table 1). There were correlation between age and

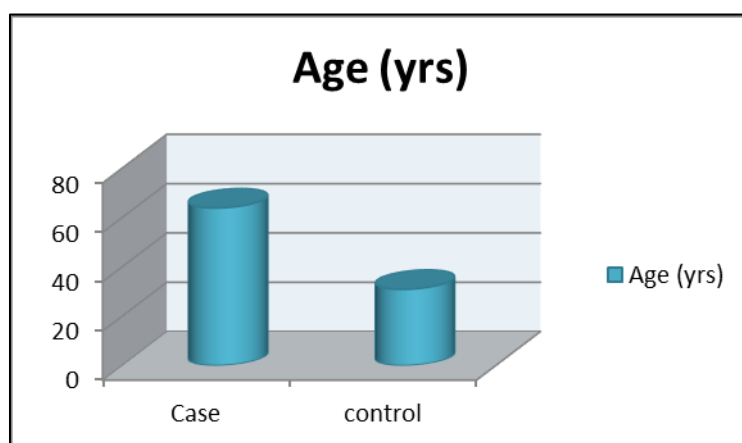
prolactin, PT, APTT & ESR but not significant ( $p>0.05$ ) (Table 2). The mean age of postmenopausal women was 64 years, while control subjects were 31 years (Fig 1).

**Table 1** Comparison of Prolactin, PT, APTT and ESR between case and control

| Parameters        | Study population |                   | P. value |
|-------------------|------------------|-------------------|----------|
|                   | case             | control           |          |
| Prolactin (ng/ml) | 12.12 $\pm$ 4.99 | 21.92 $\pm$ 12.42 | <0.001*  |
| PT (second)       | 12.69 $\pm$ 0.88 | 12.37 $\pm$ 0.58  | 0.072    |
| APTT (second)     | 34.39 $\pm$ 2.75 | 31.29 $\pm$ 3.29  | 0.044*   |
| ESR (mm/hour)     | 13.47 $\pm$ 4.79 | 14.27 $\pm$ 5.72  | 0.475    |

**Table 2** Correlation of age with prolactin, PT, APTT and ESR

| Parameters | Age (years)         |          |
|------------|---------------------|----------|
|            | Pearson correlation | P. value |
| Prolactin  | 0.104               | 0.392    |
| PT         | -0.098              | 0.422    |
| APTT       | -0.084              | 0.488    |
| ESR        | -0.159              | 0.188    |



**Figure 1** Mean age of Case and control

#### 4. Discussion

The assessment of serum prolactin in post-menopausal women has become so vital because of the increasing emphasise on the role of prolactin in the pathogenesis and progression of human breast cancer at the cellular, transgenic, and epidemiological levels. Breast cancer occurs more frequently in obese post-menopausal women. Breast cancer is also more rampant recently. Previous data had suggested that increased levels of prolactin are related to breast cancer (Pearson and Manni, 1978; Clevenger *et al.*, 2003). Prolactin has a high specificity for breast cancer, particularly the metastatic variant, making it vital for both the diagnosis and the prognosis for cancer disease (Sheth *et al.*, 1975). In our study, serum prolactin was lower in post-menopausal women compared with control subjects. A similar result was reported by Balint-peric & Prelevic. In their finding, mean serum prolactin concentrations decreased significantly during the second post-menopausal year in untreated women. Another study by Roelfsema *et al.*, reported that post-

menopausal women exhibited a 40% decrease in prolactin secretion compared with premenopausal women in the follicular phase of their menstrual cycle. Different pituitary hormone systems, like growth hormone, thyroid-stimulating hormone, adrenocorticotrophic hormone and luteinizing hormone show age, gender and body mass index-related changes. But previous study by Roelfsema *et al.*, observed Nadir prolactin concentration correlated with gender only and peak prolactin with gender and negatively with age. The finding is in line with result of the present study that found no correlation between age and prolactin. In addition, study done by Weizman *et al.*, reported no obvious correlation between elevated levels of serum prolactin and impotence. Any circumstances that lead to instability between thrombophilic and thrombosis mechanisms lead humans to either a heightened risk of bleeding or a hypercoagulable state (Nkonde-Price and Bender, 2015; Tarumi and Shinohara, 2020). When blood clots form within blood vessels, the person is at increased risk of advancing thrombogenic conditions such as deep vein thrombosis or pulmonary embolism. The higher risk of cardiovascular disease among post-menopausal women due to possible contemporary lifestyle factors such as unhealthy diet (high fat/low fiber diet), physical indolence, poor management of anxiety and other burden called for assessment of PT and APTT in this set of women. Timely diagnosis of coagulation abnormalities may be useful in the stoppage of cardiovascular complications and the choice of possible treatment plan. In the present study, APTT significantly increased in the post-menopausal women compared with control subjects. This finding is not consistent with previous reports (Schneider and Birkhauser, 2017; Ebengho *et al.*, 2022).

## 5. Conclusion

Post-menopausal women had decrease level of prolactin and increase level of activated partial thromboplastin time. The low levels of prolactin and slight increase of APTT observed in this study, suggest that routine assessment of these parameters is important, particularly for post-menopausal women.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

Authors declared that no competing interests exist

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### *Statement of ethical approval*

Study protocol was approved by Research Ethics committee of Enugu State University Teaching Hospital (ESUTH) Enugu

### *Statement of informed consent*

Each participant in this study signed an informed consent form before blood sample was collected from them.

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