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Research Article
Menopausal Phase and Iron, a Baseline Study in Calabar Cross River State, Nigeria

[1]I.M. Okafor, [2]I.N. Eze-Bassey and [2]P.D. Okon

[1]Department of Medical Lab. Science, Haematology Unit, College of Medical Sciences University of Calabar, Calabar, Nigeria
[2]Department of Medical Lab. Science, Chemical Pathology Unit, College of Medical Sciences University of Calabar, Calabar, Nigeria

Abstract

Background and Objective: Iron deficiency is one of the most prevalent nutrient disorders and women of child-bearing age are susceptible. Women's lives are marked by a continuum from intrauterine life to the elderly years and across the life span of a woman, menopause probably has the greatest impact on health. This study was aimed at providing information on the iron status and packed cell volume of pre-menopausal and post-menopausal women living in Calabar Cross River State, Nigeria. Iron parameters such as ferritin, serum iron, total iron binding capacity and transferrin saturation with iron were assayed. **Materials and Methods:** A total of 90 women were enrolled in the study, 45 pre-menopausal women and 45 post-menopausal women. Serum iron and total iron binding capacity were assayed using colorimetric method. Transferrin saturation was calculated from total iron binding capacity and serum iron while ferritin was assayed using ELISA technique and PCV was done using microhematocrit method. **Results:** The result showed significantly higher increase in ferritin level (189.79±6.83 ng mL^{-1}) of post menopausal women ($p<0.05$) when compared to pre-menopausal women (85.15$^-$115.18 ng mL^{-1}). The result further showed that serum iron and transferrin saturation with iron are significantly ($p<0.05$) higher in post-menopausal women than pre-menopausal women and that there is higher prevalence of iron deficiency in pre-menopausal women. **Conclusion:** This study has shown that post-menopausal women have higher ferritin, serum iron and transferrin saturation with iron while pre-menopausal women have higher prevalence of iron deficiency. It is important that both pre and post-menopausal women maintain an adequate iron status and follow dietary practices that enhance their wellbeing.

Key words: Menopause, iron deficiency, ferritin, post-menopause, pre-menopause

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Corresponding Author: I.M. Okafor, Department of Medical Lab. Science, Haematology Unit, College of Medical Sciences University of Calabar, Calabar, Nigeria Tel: +2348080680620

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Iron is an essential trace metal in the human diet due to its obligate role in a number of metabolic processes. In the diet, iron is present in a number of different forms, generally described as haem (from haemoglobin and myoglobin in animal tissue) and non-haem iron (including ferric oxides and salts, ferritin and lactoferrin)[1]. Iron is an essential element involved in a broad range of biologically important reactions critical for cellular function and also plays fundamental role in oxygen transport. Disorders of iron homeostasis are among the most common human disorders[2]. Iron metabolism is unusual in that it is controlled by absorption rather than excretion. Non-menstruating women lose about 1 mg of iron per day. Menstruating women lose from 0.6-2.5% more per day[3]. Iron deficiency results when iron demand by the body is not met by iron absorption from the diet, leading to Iron deficiency anaemia (IDA). In recent years, interest in the improvement of women's health has received great worldwide attention[4]. The commitment of the National Institutes of Health (NIH) and its Office of Research on Women's Health exemplifies the effort taken by the U.S. government and highlights the need for surveillance and screening programs that carefully monitor adverse effects in women[5]. The health of girls and women is affected by developmental, physiological and psychological age. Women's lives are marked by a continuum from intrauterine life to the elderly years: Infancy, childhood and adolescence, menarche, reproductive life, the menopausal transition, post-menopausal years, the elderly and frail elderly. Across the life span of a woman, menopause probably has the greatest impact[6]. Menopause is a natural aging process during which a woman passes from reproductive to non reproductive years[7]. It is traditionally defined as cessation of menstrual bleeding and is assumed to lead to an increase in iron stores over the menopausal transition[8]. Menopause typically occurs between 45 and 55 years of age[9]. This is the opposite of menarche, the time at which a woman's period start[5]. Pre-menopause refers to a woman's reproductive or fertile life, from the first menstrual period to the last. When the levels of reproductive hormones are already becoming more variable and lower and the effect of hormone withdrawal are present[10] it often starts sometimes before the monthly cycle become noticeably irregular in timing. Post-menopausal describes women who have not experienced any menstrual flow for a minimum of twelve months, assuming that they still have a uterus and are not pregnant or lactating[10]. Studies have shown that iron deficiency is prevalent in pre-menopausal women[11]. Iron deficiency in young women is relevant health issue that have received great attention from medical professional. It affects 20% of non-pregnant aged between 16 and 49 years in industrialized countries and 40% of all women in developing countries[11]. An estimated 18% of pregnant women and 9% of teens and pre-menopausal women in U.S. are iron deficient[12]. Pre-menopausal are more likely to be low in iron[13]. Due to iron losses, women with heavy menstrual bleeding may also be low in iron[14]. As women go through menopause, serum estrogen decreases and ferritin increases[13]. Estrogen decreases because of the cessation of ovarian functions, iron increase as a result of decreasing menstrual period[15]. As compared with estrogen deficiency, increased iron is an unexplored risk factor in menopausal symptoms and diseases associated with menopause[5]. Considering that current menopausal research and treatments focus mainly on ovarian hormones and their receptors, indicting increased iron as a risk factor in menopause-related diseases is more complex, yet more realistic and worth further investigation. Hence the need to evaluate the serum iron, total iron binding capacity, transferrin saturation with iron and ferritin level of pre and post-menopausal women to serve as a base line study in this locality for further research and care of menopause.

MATERIALS AND METHODS

Study area and design: This is a cross-sectional descriptive study carried out in Calabar, Cross River State, Nigeria.

Subject selection: A total of 90 women were recruited; forty five pre-menopausal women and 45 post-menopausal women were enrolled in this study. They were aged between 18 and 60 years and all resident in Calabar Metropolis. A simple random technique was used for the collection of sample and questionnaire used to record menopausal status, age, number of children, demographic and clinical data from all the enrolled subjects.

Pre-menopausal women: This group consisted of menstruating women who have not given birth and menstruating women who have given birth. The ones who have given birth, the number of children were indicated. The ages of these women were also indicated.

Post-menopausal women: This group consisted of women who have stopped menstruating. Their ages were indicated and the number of children was also indicated. Subjects from both groups were drawn from low, average and high socio-economic classes of Calabar metropolis of the Nigeria society.

Inclusion criteria: Inclusion criteria included age ≥18 years and ≤60 years, non-pregnant and willing to offer written informed consent after counselling.

Exclusion criteria: Pregnant women, women who are suffering from any form of ailment, women who did not give their consent, girls below the age of 18 years and women above 60 years were excluded from the study.

Ethical clearance: Ethical clearance for this study was sought and obtained from the Cross River State Ministry of Health Ethical Committee. The subjects gave informed consent to blood collection and the use of blood.

Sample collection and processing: Five milliliters of venous blood samples were collected, 2 mL of blood was put into a paediatric EDTA sample container while 3 mL was put into a plain sample container. The PCV was done from paediatric EDTA blood sample. Serum was separated and stored at -4°C until analyzed. Measurements of serum iron and total iron-binding capacity were performed using colorimetric method; transferrin saturation was calculated as:

$$\text{Transferrin saturation} = \frac{\text{Serum iron}}{\text{Total iron-binding capacity}} \times 100$$

The PCV was done using Microhematocrit method while Serum ferritin assay was done using enzyme immunosorbent assay (ELISA) technique.

Statistical analysis: Data obtained from this study were presented using tables, the level of significance was analyzed using student t-test and ANOVA.

RESULTS

The PCV, Serum Iron, TIBC and Transferrin Saturation of post-menopausal women were compared with pre-menopausal women as seen in Table 1. Serum iron and ferritin levels were significantly higher in post-menopausal women (84.13±38.73, 189.79±6.83) compared to pre-menopausal women (65.02±31.76, 85.15±115.18) p-value = 0.012 and 0.004, respectively. Table 2 showed mean serum iron, TIBC, transferrin saturation and ferritin level of post-menopausal women based on number of years after menopause. Table 2 showed that serum iron, TIBC, transferrin saturation with iron and ferritin level increased as the years of post-menopause increased even though the differences were not statistically significant.

Table 3 showed serum iron, TIBC, transferrin saturation and ferritin level of post-menopausal women based on number of children. Serum iron, TIBC, transferrin saturation and ferritin level were shown to decrease as the number of children by the pre-menopausal women increased. Table 3 also showed that these iron parameters were significantly reduced in women that had 4 children and above when compared to other women.

Table 4 showed prevalence of iron deficiency in post-menopausal women and pre-menopausal women using transferrin saturation and serum ferritin as a marker. Table 4 showed that iron deficiency was significantly higher among the pre-menopausal women when using both transferrin saturation with iron (55.6%, p = 0.005) and ferritin (24.4%, p =0.004) as markers compared to postmenopausal women.

DISCUSSION

This study observed that serum iron and ferritin levels were significantly higher in post-menopausal women

Table 1: PCV, serum Iron, TIBC and transferrin saturation of pre-menopausal and post-menopausal women

Parameters	Pre-menopausal (n = 45)	Post-menopausal (n = 45)	p-value	Remarks
PCV (L L^{-1})	0.36±0.04	0.39±0.05	0.078	NS
Serum iron (μg dL^{-1})	65.02±31.76	84.13±38.73	0.012	S
TIBC (μg dL^{-1})	358.71±69.96	371.51±63.79	0.366	NS
Transferrin saturation (%)	19.62±9.20	22.98±9.06	0.085	NS
Ferritin (g mL^{-1})	85.15±115.18	189.79±6.83	0.004	S

S: Significant difference, NS: No significant difference

Table 2: Serum Iron, TIBC, transferrin saturation and ferritin of post-menopausal women based on number of years after menopause

	Period after Menopause		
Parameters	≤1year (n = 13)	≥2 years (n = 30)	p-value
Serum iron (μg dL^{-1})	70.00±29.18	91.26±41.92	0.105
TIBC (μg dL^{-1})	381.61±59.49	372.78±66.01	0.683
Transferrin saturation (%)	19.23±8.36	24.46±9.50	0.33
Ferritin (ng mL^{-1})	186.85±181.38	219.03±238.54	0.745

S: Significant difference, NS: No significant difference

Table 3: Serum iron, TIBC, transferrin saturation and ferritin of premenopausal women based on number of children

Parameters	Without children (n = 23)	≤3 children (n = 13)	≥4 children (n = 9)	p-value
Serum iron (μg dL^{-1})	72.82±36.17	66.07±24.52	43.55±18.80*	0.030
TIBC (μg dL^{-1})	364.30±50.39	361.15±93.19	340.88±80.35*	0.043
Transferrin saturation (%)	21.70±10.16	20.62±7.74	12.88±5.20*	0.042
Serum ferritin (ng mL^{-1})	99.20±142.10	86.29±6.43	47.75±29.00*	0.019

S: Significant difference, NS: No significant difference

Table 4: Prevalence of iron deficiency based on transferrin saturation with iron and ferritin level of pre and post-menopausal women

Parameters	Pre-menopausal women (n = 45)	Post-menopausal women (n = 45)	p-value
Prevalence of iron deficiency (transferrin saturation)	25 (55.6%)	16 (35.6%)	0.005
Prevalence of iron deficiency (ferritin)	11(24.4%)	4 (8.9%)	0.004

compared to pre-menopausal women which agreed with the study carried out by Sullivan[16] and Erahbor *et al.*[6]. Serum iron is the measure of how much iron is in serum, post-menopausal women conserve iron as menstrual cycles and periods discontinue, since the major route of iron loss is by blood loss, this may account for the increase in serum iron of post-menopausal women. Ferritin is the major storage form of iron in the body and it is an acute phase reactant. In pre-menopausal women, there are physiological process that leads to loss of iron at intervals such as menstruation, pregnancy and lactation. Following loss of iron, the stored iron is depleted to be mobilized for red cell production and for body's metabolic processes. This may result in decrease ferritin level in pre-menopausal women. The natural biologic system in young women is high estrogen and low iron. The reverse is true in older women: Low estrogen and high iron as shown by high level of ferritin observed among post-menopausal women in this study. Studies have shown that increased iron could lead to oxidative stress and sensitize the skin to UV exposure. Urinary levels of 8-oxo-2'-deoxyguanosine, a marker of oxidative DNA adducts, has been shown to increase with serum ferritin levels in men and women[17]. Because iron is a growth nutrient, increased iron could also increase proliferation of osteoblast progenitors without differentiation to mature osteoblasts and thus, slow bone formation[5].

Packed cell volume and total iron binding capacity are increased in post-menopausal than pre-menopausal in agreement with work done by Achie *et al.*[18] which recorded increased packed cell volume among post-menopausal women and world health organization[19] which stated that low iron values in conjunction with elevated TIBC values yielding less than 16% transferrin saturation, generally indicate iron-deficiency anaemia. There was significantly high value of transferrin saturation value in post-menopausal women compared to pre-menopausal women which indicates higher prevalence of iron deficiency among pre-menopausal women when compared to post-menopausal women. Anaemia is a major public health concern worldwide, especially among women and children. Iron deficiency anaemia was higher among pre-menopausal women compared to post-menopausal women. This finding is consistent with that of Wang *et al.*[14]. According to world health organization[19], the most common cause of iron deficiency anaemia in women of childbearing age are heavy menstrual bleeding and blood loss during child birth, this may explain the higher prevalence of iron deficiency obtained among pre-menopausal women. These finding is accordance with other studies[20,21].

CONCLUSION

This study has shown that serum iron, ferritin and transferrin saturation with iron are increased in post-menopausal women. It also showed that pre-menopausal women have higher incidence of iron deficiency compared to post-menopausal women. Pre-menopausal women need to consider their iron intake. It is important to increase these women's knowledge of iron-rich foods and the dietary constituents that enhance and inhibit the absorption of nonheme iron through increase awareness. More studies shouldalso be encouraged in this area in order to understand the role of increased iron in menopause and postmenopause.

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