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Changes in Haematological Indices of Women at Different Fertility Periods in Nnewi, South-East, Nigeria

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Abstract

Background: Menstruation and menopause have both been shown to significantly affect the concentration of a number of biologically important plasma constituents, including blood counts.
Objective: To evaluate the haematological indices of menstruating, premenopausal and menopausal women in Nnewi with a view to establishing possible effects of menstruation and menopause on counts.
Materials and Methods: One hundred and eighty women; comprising 60 menopausal (aged 50-75 years), 120 pre-menopausal (60 aged 20-35 years, who were not menstruating at the point of recruitment and 60 who were menstruating at the period of testing) were recruited by simple random sampling. Socio demographic and other data was collected from each participant with the aid of a questionnaire while 2mls of venous blood was collected (following standard protocols) into ethylene diamine tetra acetic acid (EDTA) specimen container for full blood count estimation, using Prokan® haematology auto-analyzer. Data analysis was done using the statistical package for social sciences (SPSS) version 20) computer software, results were expressed as means ±SD, while associations between variable were explored using the student t-test and analysis of variance.Ethical clearance was obtained from our institutional review board and all participants gave informed consent.
Results: The red blood cell count (RBC) was significantly higher in both menstruating and non-menstruating pre-menopausal women. The platelet count was however significantly higher in menstruating women. The white cell count (WBC), mean cell volume (MCV) and mean cell haemoglobin (MCH) were significantly higher in menopausal subjects.
Conclusion: The menopausal period could offer some protection against subclinical haemoglobin depletion in our population.

Keywords: Blood counts, red cell indices, menstruation, premenopausal, menopausal women, Nnewi.

INTRODUCTION

Physiological variations have been observed in several parameters (including blood count) in the human body as part of the normal circadian rhythm, which could be seasonal or diurnal.[1]In pre-pubertal humans, no major differences were observed between gender in red blood cell count, haemoglobin (Hb) or even serum ferritin concentration.[2] However, after the onset of menstruation specific differences in gender become apparent but usually reverts to the pre-pubertal levels at the fifth decade of life, after menopause would have occurred.[3] The human menstrual cycle involves complex and regular anatomical and physiological changes over an approximate monthly time periods under the control of the hypothalamic-pituitary-ovarian (HPO) axis.[4] The endometrium is stimulated and regulated by the ovarian steroid hormones (estrogen and progesterone) which in turn are controlled by an integrated HPO axis, through the release of follicle stimulated hormone (FSH) and luteinizing hormone (LH).[4] The activities and associated fluctuations in the levels of these hormone leads to the different phases encountered in the menstrual cycle divided into; the menstrual, follicular/ovulatory, and luteal phases.[4]

Menopause is defined as the permanent cessation of menstruation due to loss of ovarian follicular activity.[5] This results in a decrease in estrogen secretion which is responsible for most of the features seen in menopausal women.[6] Correspondingly, the pre-menopause period is said to commence when a woman enters the reproductive years and finishes with the notice of the first sign of menopause.[7] This period is quite distinct from the peri-menopausal period, which is defined as the time before and after the last period, also referred to as the menopause transition years.[8] During this period, the hormone levels are said to fluctuate erratically but has not yet completely ceased.[6]

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Cruikshank had earlier reported a progressive and significant increase in haemoglobin concentration in women into the fifth decade of life; this finding was attributed to the hormonal environment of menopause.[9] Similarly, Nakada *et al.* reported that oestrogen administration significantly increased the division and proliferation of haematopoetic stem cell (HSCs) and thus explains the higher blood counts in women during the reproductive years.[10] It is therefore likely that the cessation of menstruation at menopause could be an additional boost to haematological parameters in women, particularly in areas with high burden of nutritional anaemias. In keeping with this line of thought, the report of Achie *et al.* showed high red cell count, haemoglobin concentration and haematocrit in menopausal women in Zaria, North Central Nigeria, in addition to significant increase in the mean cell volume (MCV) in their subjects who were > 10 years post menopause.[11] The study equally identified that the increase in MCV could herald macrocytic anaemia in menopausal women in this region of the country and recommended further evaluation for serum folate and B_{12} levels.[11] Platelet count has been reported to decrease in women at about the time of onset of menstruation, followed by a later rise.[12] The initial decrease in count is thought to be due to the rupture of blood vessels which occurs with onset of menstruation, followed by aggregation of the platelets at the sight of rupture and exacerbated platelet activation ultimately leading to platelet consumption.[12]

There is paucity of literature on the effect of menopause on haematological parameters in women from South-east Nigeria, this study was therefore aimed at evaluating and comparing the heamatological profile of premenopausal and menopausal women in Nnewi, South-east Nigeria.

SUBJECTS AND METHODS

Study Design

A total of 180 subjects were recruited for the study using simple random sampling technique. These were grouped into three categories: of 60 women each: menopausal (aged 50-75 years), pre-menopausal non menstruating and menstruating subjects (aged 20-35 years in both categories). The inclusion criteria involved post menopausal women who are at least 1 year amenorrhoeic due to a natural cause without a hysterectomy or other procedure that would have stopped their menses, [6] and pre-menopausal women who were regularly menstruating, non-lactating, non-pregnant with no use of hormonal contraception for at least 1 year. Those who were diabetic, hypertensive, smokers, alcohol consumers and a history of recent blood transfusion or were on medication were excluded from the study. Questionnaires were used to assess the subjects' eligibility for the study. Each subject had 2ml of blood collected into EDTA container, and was analyzed immediately using Prokan® haematology auto-analyzer.

Study Area

The study was carried out in Nnewi North and South local government area of Anambra State in south eastern Nigeria. The official languages spoken by the people are Igbo and English.The total population of people living in Nnewi is 391,227; while the population of women living in Nnewi who are between the ages of 20-65 years is 86,960.[13]

Ethical Consideration:

Ethical approval was obtained from the institutional ethics committee. Written informed consent was obtained from the patients according to Helsinki declaration on research involving human subjects.

Statistical Analysis:

The data obtained was analyzed using statistical package for social science (SPSS) version 20 (SPSS Inc.,Chicago, IL, USA). The result was expressed as mean ± standard deviation (SD). Differences between two variables were determined using students't-test, while differences between more than two variables were determined using one way analysis of variance (ANOVA); level of significance was set at $P < 0.05$.

RESULTS

The red cell count (RBC), packed cell volume (PCV) and haemoglobin concentration were significantly lower in menstruating compared with menopausal and premenopausal categories ($4.85 \pm 0.05 \times 10^{12}$/L vs. $4.85 \pm 0.57 \times 10^{12}$/L vs. $5.29 \pm 0.86 \times 10^{12}$/L and 36.92 ± 4.71 L/L vs. 39.08 ± 5.44 L/L vs. 39.09 ± 6.03 L/L, and 123.06±12.56 g/L vs. 130.12±32.19 g/L vs. 130.37±17.55 g/L, p values <0.001, 0.04, and 0.04 respectively, Table 1). Correspondingly, the total white cell count (TWBC) was significantly higher in menopausal compared with menstruating and premenopausal groups ($6.20 \pm 1.61 \times 10^{9}$/L vs. $5.93 \pm 1.41 \times 10^{9}$/L vs. $5.04 \pm 0.86 \times 10^{9}$/L, respectively, p<0.001, Table 1) The platelet count was significantly higher in menstruating compared with premenopausal and menopausal women (p = 0.01, Table 1).

The RBC and TWBC were not significantly different in menstruating compared with menopausal women but were in other women subgroups (Table 2). Correspondingly, the platelet count was observed to be significantly different when compared between premenopausal and menstruating women but not in other categories (Table 2).

The mean cell volume (MCV) and mean cell haemoglobin (MCH) were significantly higher in menopausal women compared to other women groups (p<0.001, respectively, Table 1)

The MCV and MCH were not significantly different in premenopausal and menstruating categories but were in other subgroups of women studied (Table 2).

Blood count and red cell indices were not significantly different among different age groups in premenopausal, menstruating and menopausal categories (p values all >0.05).

DISCUSSION

Estrogen has long been associated with the inhibition of erythropoiesis and a diminished levels of this hormone (as seen in menopausal women) was reported to be associated with increased haemoglobin levels. [14,15] In contrast, recent evidence appears to suggest that estrogen might equally have a stimulant effect on haematopoiesis by increasing the proliferation of stem and progenitor cells. [16]

In this study, we observed that premenopausal women had significantly higher red blood cell count (RBC) as compared to menstruating and menopausal women (p <0.001, Table 1), while the PCV and haemoglobin concentration were significantly lower in menstruating women but comparable in the premenopausal and menopausal sub groups (p = 0.04, respectively, Table 1). Previous report had suggested that haemoglobin concentration may decrease in menopausal women, mainly due to high prevalence rates of nutritional anaemias in the elderly.[11] This was contradicted by the report of Milman *et al.*, which indicated that haemoglobin concentration may actually be higher in menopausal women, most probably due to the cessation of menstruation.[16] Even though this study recorded an increase in the haemoglobin level in menopausal and premenopausal women compared with the menstruating group, these differences were not statistically significant on post-hoc analysis (Table 2).

The mean total white blood cell count (TWBC) in this study was significantly higher in menopausal compared with other women groups (p<0.001, Table 1). More so, the TWBC count was significantly higher in menstruating compared with non-menstruating premenopausal women (p<0.001, Table 2). This observation is in agreement with an

earlier report which showed that significant increase in the total white cell count (TWBC) occurred at the onset of menstruation, compared with controls.[17] This increase was thought to be as a result of the peripheral mobilization of leukocytes as part of the acute stress of menstruation.[4] The levels of TWBC has been shown to increase with age, particularly in women,[18] this may thus explain significant increase in TWBC count observed in menopausal compared with premenopausalcategory in this study (p<0.001, Table 2).

A significantly higher mean platelet count was observed in menstruating women, compared to other women groups (p = 0.01, Table 1). Importantly, the platelet was equally significantly higher in menstruating compared with premenopausal women (p<0.001, Table 2). These observations have been emphasized in an earlier study which suggested that increased platelet counts observed in menstruating women was a compensatory response to endothelial vascular rupture in order to facilitate effective haemostasis in the endometrium.[12]

There was a statistically significant increase in the mean corpuscular volume (MCV) and the mean corpuscular haemoglobin (MCH) of menopausal women when compared with that of the premenopausal and menstruating women (p<0.001, Table 1). This difference persisted when levels were compared between menopausal vs. premenopausal women and menopausal vs. menstruating women (p<0.001, respectively, Table 2). Even though the increase in MCV did not extend into the macrocytic range, it is important to observe that these increases were observed to occur progressively from the microcytic to the normal range, from premenopausal to the menopausal study groups (Table 1). It may thus appear that our study population might have had pre-existing subclinical microcytic anaemia which then became corrected with the onset of menopause, leading to significant increases in MCV and MCH. This line of thought appears to be favoured by the documented high prevalence of microcytic anaemia (especially iron deficiency) in the environment of this research.[19] Pre-existing iron depletion/deficiency stands to be exaggerated by the monthly blood loss that occur from menarche till the onset of menopause in women. Previous studies among Nigerian and Caucasian women populations supported our observation.[11,20] Interestingly, the Nigerian study observed increases in MCV even up to the microcytic range in menopausal women and concluded that this may be due to concurrent nutritional (B12/folate) insufficiency.[11] It will be interesting to evaluate for the true prevalence of nutritional anaemia in our pre- and post menopausal women population in a subsequent follow-up study.

Table 1: Comparison of means (±SD) of blood count and red cell indices in women at different fertility periods

Haematological Parameters	Premenopausal Women(Mean±SD)	Menstruating women(Mean±SD)	Menopausal women(Mean±SD)	P-value
RBC (× 10^{12}/L)	5.29±0.86	4.85±0.05	4.85±0.57	<0.001*
PCV (L/L)	39.09±6.03	36.92±4.71	39.08±5.44	0.04*
HB (g/L)	130.37±17.55	123.06±12.56	130.12±32.19	0.04*
TWBC (× 10^{9}/L)	5.04±0.86	5.93±1.41	6.20±1.61	<0.001*
Platelet count (× 10^{9}/L)	219.72±48.60	239.00±45.35	229.08±54.30	0.01*
MCV(FL)	74.11±6.92	76.10±8.38	80.37±6.23	<0.001*
MCH(pg)	21.84±2.31	22.04±2.29	23.42±2.18	<0.001*
MCHC(g/L)	295.13±26.29	289.75±16.33	291.28±17.19	0.33
Lymphocytes (%)	46.47±5.85	46.87±7.84	45.67±10.11	0.72
Granulocytes (%)	45.45±7.00	44.30±8.19	51.81±9.61	0.36

Key: *significant p values, RBC = red blood cell, PCV = packed cell volume, HB = haemoglobin concentration, TWBC = total white blood cell, MCV = mean corpuscular volume, MCH = mean corpuscular haemoglobin; mean corpuscular haemoglobin concentration (MCHC).

Table 2: LSD Post-hoc analysis of blood count and red cell indices in various categories of women.

Haematological Parameters	Premenopausal vs Menstruating women (p- value)	Premenopausal vs Menopausal women (p- value)	Menstruating vs Menopausal women (p- value)
RBC (× 10^{12}/L)	<0.001*	<0.001*	0.97
PCV (L/L)	0.30	0.99	0.31
HB(g/L)	0.57	0.28	0.10
TWBC (× 10^{9}/L)	<0.001*	<0.001*	0.27
Platelet count (× 10^{9}/L)	<0.001*	0.05	0.30
MCV (FL)	0.13	<0.001*	<0.001*
MCH (pg)	0.63	<0.001*	<0.001*
MCHC (g/L)	0.15	0.30	0.68
Lymphocytes (%)	0.79	0.59	0.42
Granulocytes (%)	0.84	0.26	0.19

Key: *significant p values, RBC = red blood cell, PCV = packed cell volume, HB = haemoglobin concentration, TWBC = total white blood cell, MCV = mean corpuscular volume, MCH = mean corpuscular haemoglobin; mean corpuscular haemoglobin concentration (MCHC).

CONCLUSION

The lower haematocrit observed in the study population during menstruation is believed to be related to blood loss, additionally, this study established that menopause is associated with a significant increase in the red cell indices. While we believe that this finding may be related to possible pre-existing nutritional anaemia in our population of premenopausal and menstruating women, which became corrected with cessation of menstruation at menopause,it is important that this observation is further validated in follow up studies, so as to enable possible institution of epidemiological interventional programmes that could address it.

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