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Review Article

Immunohaematological Changes in Perimenopausal and Menopausal Nigerian Women: A Review

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Abstract
During the menopause and perimenopause periods, a woman's hormone levels, especially those of oestrogen and progesterone, begin to fall dramatically. Immune competence, haematological parameters, and autoimmune disease and infection susceptibility are all impacted by these hormonal shifts. The menopausal transition is particularly challenging for Nigerian women because of the country's high rate of infectious diseases, dietary deficits, genetic diversity, and lack of access to healthcare. The present state of knowledge on immunohaematological alterations in Nigerian women during perimenopause and menopause is reviewed in this review. It draws attention to changes in infections, autoimmune risk, cytokine balance, coagulation, anaemia, and immunological response. The article points out where studies are lacking in the areas of cytokine profiling, autoimmune monitoring, interactions between genes and the environment, and psychosocial factors. Reducing morbidity and enhancing quality of life in Nigeria requires strengthening research capacity and integrating immunohaematological surveillance into women's health care.

Keywords: Menopause, Perimenopause, Nigeria, Immunohaematology.

Introduction

Endocrine, metabolic, and immune system changes accompany menopause, which is characterised by the permanent end of menstruation when ovarian follicular activity has been lost. Menopause often begins between the ages of 48 and 50 in Nigerian women, which is slightly younger than in Western cultures [1] Perimenopause, the transitional phase, typically starts in the mid- to late-40s. There is evidence that menopause can lead to a number of health problems, including "inflammaging," anaemia, changes in coagulation, decreased immunological surveillance, and an increased risk of infections and autoimmune diseases [2] But in Nigeria, these shifts take place within a tangled web of factors, including dietary deficits, high rates of maternal morbidity and TB, hepatitis, malaria, and HIV/AIDS, as well as a lack of adequate diagnostic facilities. Regardless, immunohaematological abnormalities among Nigerian women going through menopause have only been the subject of a small number of studies[3].

An important biological milestone in women's life is menopause, which is the permanent end of menstruation when ovarian follicular activity has been lost. After twelve months of no menstruation and no other obvious medical reasons, a clinical diagnosis is made. Menstrual cycle irregularities, hormone level fluctuations, and a host of physical and mental health issues characterise the perimenopause, the time just before menopause. Researchers in Nigeria have found that menopause typically begins between the ages of 47 and 49, far earlier than the worldwide average of 51 years [4]

A number of systems, including reproductive organs and regulatory networks, are involved in the menopausal transition. Widespread immunohaematological alterations are put in motion by the fall of oestrogen and progesterone, two hormones with well-documented functions in immunomodulation and haematoiesis. By regulating cytokine expression, bolstering

vascular and bone marrow integrity, and increasing B-cell antibody production, oestrogen improves innate and adaptive immune responses [5]. In addition to increasing the risk of infections and autoimmune diseases, its absence leads to a pro-inflammatory state, decreased haemopoiesis, and increased oxidative stress.A worldwide view on the immune system and menopause "Inflammaging" is a condition of chronic, low-grade inflammation driven by increased cytokines like interleukin-6 (IL-6), tumour necrosis factor alpha (TNF-α), and C-reactive protein (CRP), which has been linked to menopause worldwide. Reduced T-cell function, decreased vaccination responsiveness, and worse infection control are all symptoms of immunosenescence, which is defined as the progressive deterioration of immunological competence with age [6]. The incidence of non-communicable disorders, including metabolic syndrome, osteoporosis, and cardiovascular disease, increases dramatically after menopause due to these immunohaematological alterations. Double burden of disease in the Nigerian context. Contextual variables in Nigeria further shape the immunohaematological landscape of menopause. Women in Nigeria endure the twin whammy of communicable and non-communicable diseases, in contrast to high-income nations where menopause is mostly researched in relation to non-communicable illnesses. Midlife and older women are disproportionately impacted by endemic infectious diseases as HIV/AIDS, malaria, TB, and viral hepatitis [7]. At the same time, changes in nutrition, lifestyle, and urbanisation are contributing to the epidemic of non-communicable diseases such as obesity, hypertension, and diabetes [8].

These epidemiological facts interact with the menopause drop in hormonal and immune protection, which increases health hazards. Issues of culture and socioeconomic status.In addition to biological factors, cultural and socioeconomic factors impact menopausal symptoms in Nigeria. How women experience and react to menopause changes is influenced by factors such as healthcare accessibility, poverty levels, gender inequality, and strongly held cultural beliefs. Some women see menopause in a good light, seeing it as a release from having to have children, while others see it negatively, as a sign of getting older, being weaker, or having less social standing [9] There is a lack of local data on immunohaematological outcomes because of these beliefs, which influence people's health-seeking behaviour and their involvement in research. Is immunohaematology the area of focus? Researching immunohaematological alterations in Nigerian women going through menopause is significant from a scientific and therapeutic perspective. This population is understudied in Nigeria despite the prevalence of conditions such as anaemia, lymphocyte decrease, altered cytokine patterns, autoimmune disorders, and coagulation abnormalities. Advanced immunological tests including cytokine profiling and autoantibody screening are typically only available at tertiary centres, while laboratory investigations typically centre on basic haematological indices [10].

Appropriate clinical care and thorough knowledge are impeded by this diagnostic gap. With a focus on the Nigerian setting, this review compiles current information on the immunohaematological profile of women during perimenopause and menopause, and it draws attention to research gaps that need to be addressed immediately. The main reason why women go through immunohaematological changes during perimenopause and menopause is because of the decrease in ovarian hormones, especially oestrogen and progesterone. Hormones have far-reaching impacts on immunology and haemopoiesis in addition to their reproductive roles. Their depletion triggers a series of cellular and molecular changes that explain why menopausal women are more prone to infections, autoimmunity, anaemia, and coagulation problems.

2.1.1 The Role of Oestrogen

The role of Oestrogen in Immune Mediating T lymphocytes, B lymphocytes, macrophages, and dendritic cells are immune cells that express oestrogen receptor beta (ERβ) and oestrogen receptor alpha (ERα), the nuclear receptors that regulate the immune system [11] Oestrogen, in physiological amounts, improves immune surveillance through: Oestrogen promotes humoral immunity by increasing the synthesis of antibodies, specifically immunoglobulin G (IgG) and immunoglobulin A (IgA), and by increasing the proliferation of B-cells. It modulates cytokine responses by increasing levels of cytokines that inhibit inflammation, like IL-4 and IL-10, and decreasing levels of cytokines that promote inflammation, including TNF-α and IL-6. Oestrogen helps the immune system fight off invaders by making mucosal surfaces more barrier-like and increasing the phagocytic activity of macrophages[12].This delicate equilibrium is upset when oestrogen levels drop during menopause. The outcome is a change towards an overarching pro-inflammatory state, marked by heightened production of IL-1, IL-6, and TNF-α. Postmenopausal women are more likely to suffer from metabolic problems, osteoporosis, and cardiovascular disease as a result of this chronic, low-grade inflammatory state, which is sometimes referred to as "inflammaging"[13].

2.2 Oestrogen and Immune System Tolerance

Although progesterone is most recognised for its function in sustaining pregnancy, it also has important immunoregulatory effects. Immune tolerance is enhanced by it through: By preventing the growth of T cells, Stimulating the production of regulatory T-cells , Lowering the activity of natural killer (NK) cells, Reducing the generation of cytokines that promote inflammation In women who are trying to conceive, these effects help keep the immune system from going into overdrive and causing autoimmunity. Immune dysregulation is exacerbated by the loss of progesterone during menopause, which eliminates this protective barrier. Research in reproductive immunology conducted in Nigeria has shown that older women who do not get enough progesterone may be more likely to develop autoimmune thyroid illness and systemic lupus erythematosus [14].

2.3.1 Hormones and Blood Cell Production

Ovarian hormones affect immunological control, bone marrow function, and haemopoiesis. Oestrogen promotes the synthesis of red blood cells by increasing the susceptibility of bone marrow to the hormone erythropoietin. Menopausal women are at increased risk for anaemia due to a decline in erythropoietic drive caused by oestrogen deficiency; this risk is magnified in Nigeria, where both dietary inadequacies and chronic illnesses are common [15].Oestrogen influences both the generation and function of platelets. It decreases platelet aggregation by increasing endothelial nitric oxide production. Postmenopausal women, especially those with cardiovascular risk factors like hypertension or diabetes mellitus, have an increased risk of thromboembolic events because to the increased platelet reactivity caused by its reduction.

2.4 Vascular Health, Oestrogen, and Coagulation

Among estrogen's many important but underappreciated functions is its impact on the coagulation cascade. In contrast to coagulation factors like fibrinogen, oestrogen increases the synthesis of fibrinolytic proteins such tissue plasminogen activator. As a result, the equilibrium shifts towards a hypercoagulable state due to decreased oestrogen. There is an elevated risk of thromboembolic problems in obese or hypertensive postmenopausal women from Nigeria, as evidenced by higher fibrinogen levels and greater D-dimer [16].

2.5.1 Molecular Processes: Signal Transduction Routes

Oestrogen regulates multiple critical pathways at the molecular level: NF-κB pathway: In a typical scenario, oestrogen prevents inflammation by preventing NF-κB activation. This inhibition is lost as oestrogen levels drop, leading to an increase in inflammatory signalling. To regulate cytokine responses, particularly IL-6 and interferon signalling, oestrogen interacts with the JAK/STAT signalling system. Oestrogen regulates antioxidant enzymes including superoxide dismutase, which helps with oxidative stress. Reduced levels cause oxidative stress, which in turn harms immunological cells and RBCs even more. The balancing effects of progesterone include regulating dendritic cell activity and Toll-like receptor signalling. These molecular findings shed light on the ways in which the immune system is fundamentally altered after menopause [17].

2.6 The Early Hormonal Decline and Compounded Risk in the Nigerian Context

Consideration of context is necessary when attempting to understand the hormonal basis of immunohaematological alterations in women from Nigeria. Menopause typically begins at a younger age in Nigerian women compared to women in Western countries. Iron, folate, vitamin D, and vitamin B12 deficiencies, a high prevalence of chronic infections (HIV, malaria, tuberculosis, hepatitis), and genetic factors (such as sickle cell trait) already compromise immune and haemostatic health, and this earlier decline in oestrogen and progesterone compounds these problems. As a result, menopause in Nigeria may have an earlier, more noticeable, and clinically important immunohaematological impact than the average worldwide [3].

Hormone replacement therapy (HRT) restores oestrogen and progesterone levels, which alleviates numerous immunohaematological effects of menopause. It mitigates the effects of osteoporosis while simultaneously enhancing hemotopoiesis and decreasing pro-inflammatory cytokines. Cost, accessibility, education, and cultural beliefs about menopause as a natural process that does not necessitate intervention all contribute to the incredibly poor uptake of HRT in Nigeria [18]. Hormonal or non-hormonal alternatives must be researched immediately if they are to be safe, inexpensive, and culturally acceptable. Blood Molecular Alterations in Nigerian Women During Menopause and Perimenopause The hormonal changes that occur during perimenopause and menopause have several important clinical repercussions, one of which is a reduction in haemoglobin levels. Red blood cell indices, white blood cell counts, and platelet activity are all impacted by the drop in ovarian hormones, which in turn impacts erythropoiesis, leukopoiesis, and thrombopoiesis. Nutritional deficits, chronic diseases, and socio-economic factors further exacerbate these haematological alterations in Nigeria, making them a vital topic of study.

3.1 The Dynamics of Anaemia and Red Cells

In Nigerian women, anaemia is a prevalent haematological change that often occurs during and after menopause. A number of processes are involved: Hormonal withdrawal: reduced red cell synthesis is caused by estrogen's drop, which promotes erythropoietin sensitivity. Inadequate nutrition: Inadequate iron, folate, and vitamin B12 intake is associated with megaloblastic anaemia and iron deficiency in Nigerians [19] Anaemia due to chronic disease is prevalent in elderly Nigerian women and is caused by chronic infections like as malaria, helminthiasis, HIV, and tuberculosis. Anaemia is worsened by chronic kidney disease (CKD), which is more common in postmenopausal women who also have diabetes and hypertension. CKD hinders the generation of erythropoietin [20]. Researchers in South-West Nigeria found that compared to premenopausal women, postmenopausal women tended to have lower levels of haemoglobin (Hb), packed cell volume (PCV), and mean corpuscular volume (MCV) .Fatigue, decreased work capability, and worse quality of life are clinical manifestations of these changes.

3.2 Immunosenescence and Changes in White Blood Cells

Menopause hastens the ageing process, which already causes a gradual deterioration in the immune system. Alterations to the number and function of white blood cells are a haematological indicator of immunological ageing. Reduced CD4+ and CD8+ T-lymphocyte counts in perimenopausal women compared to reproductive-age women represent immunosenescence, according to studies conducted in Nigeria [5] Predominance of neutrophils: As oestrogen levels drop, the body's immune system becomes more prone to inflammation, which in turn increases the risk of cancer and cardiovascular disease . Increased monocyte activity and the release of pro-inflammatory cytokines are symptoms of menopause that can lead to systemic inflammation that lasts throughout the body. These alterations clarify why wound healing and infection vulnerability (such as UTIs and pneumonia) are worse in postmenopausal women. This kind of immune system decline is very concerning for public health in Nigeria, a country with an already high burden of infectious diseases.

3.3 Alterations to Haemostasis and Platelet Function

The loss of oestrogen has a profound effect on coagulation factors and platelets. The changes in blood types encompass: A higher risk of thrombosis is associated with increased platelet reactivity, as seen by higher platelet counts and aggregation indices in postmenopausal women from Nigeria [21]. Postmenopausal women are at a higher risk of venous thromboembolism and stroke due to their hypercoagulable state, which is shown by elevated fibrinogen, D-dimer, and clotting factor VIII levels [2] Oestrogen shortage decreases tissue plasminogen activator levels, which in turn decreases the body's fibrinolysis, or the process by which clots are broken down. The growing prevalence of hypertension, diabetes, and obesity among Nigerian women makes these findings clinically significant. These conditions, in conjunction with menopause-induced coagulopathy, contribute to the high rate of cardiovascular mortality in this population.

3.4 Lean Body Mass and Deterioration with Age

Another aspect impacting haematological health in postmenopausal women is the age-related reduction in bone marrow reserve. There is a decline in the stromal cell and growth factor microenvironment that promotes haemopoiesis in the bone marrow. Along with a decrease in oestrogen stimulation, this causes: The number of reticulocytes is low. Decreased ability to deal with anaemia .Changes in the ratio of myeloid to lymphoid cells. Because chronic infections and malnutrition are more common in Nigeria, which speeds up the exhaustion of bone marrow, this decrease may be more noticeable in Nigerian women [22]

3.5 Genetic and Trait Considerations in Sickle Cell Disease

Menopausal women in Nigeria have distinct haematological patterns due to the high incidence of sickle cell trait and disease. There is a correlation between sickle cell trait and lower haemoglobin and greater haemolysis in postmenopausal women, and anaemia, vaso-occlusive crises, and thromboembolic events are more common in sickle cell diabetes. Studying menopause-related haematology in Nigerian women is unique due to the interaction of these hereditary variables with hormonal decline.

3.6 Typical Changes to Laboratory Parameters

Among the routine haematological parameters utilised to evaluate Nigerian women in the perimenopausal and menopausal stages are: Hb, PCV, MCV, RDW, means corpuscular haemoglobin, and mean corpuscular volume are all red cell indicators. White cell indices: Total WBC, differential counts, CD4/CD8 subsets, and inflammatory indicators (NLR, platelet-to-lymphocyte ratio). Indicators of platelets: counts, MPV, and PDW (platelet distribution width). Thrombocytopenia, fibrinogen, activated partial thromboplastin time (aPTT), and D-dimer coagulation panel. [23]

3.7 The Situation in Nigeria and Its Effects on Public Health

A larger socioeconomic and epidemiological framework is necessary to understand the haematological alterations in Nigerian women throughout perimenopause and menopause: Many cases of anaemia or clotting abnormalities go untreated until they are severe because of limited access to healthcare. Cultural views of menopause as an inevitable part of life can make people reluctant to seek medical help. Laboratory results might be more difficult to interpret when overlapping with viral disorders like HIV and malaria, each of which can affect haematological indices in its own way. Screening menopausal women for anaemia, coagulation problems, and immunosenescence should be a priority in public health policies and community health programs.

4. Changes in Immunology in Nigerian Women During Menopause and Perimenopause

Both the reproductive system and the immunological system undergo significant changes after menopause. In women, immunological senescence, chronic inflammation, autoimmune risk, and decreased response to infection are all made worse by the fall of oestrogen and progesterone, which changes both the innate and adaptive immune processes. These immunological alterations are worsened in Nigerian women because they happen in a context with a high prevalence of infectious diseases, poor nutrition, and inadequate access to preventative healthcare [24].

4.1 Immunosenescence and "Inflammaging"

Immunosenescence refers to the structural and functional deterioration of the immune system that occurs with ageing and menopause. This is what makes it unique: Thymic involution causes a decrease in the production of naïve T-cells. Memory and senile T-cell accumulation Decrease in antibody affinity and diversity of B-cells. Difficulty presenting antigens Inflammaging occurs when estrogen's anti-inflammatory effects are lost, which is characterised by higher levels of IL-6, TNF-α, and C-reactive protein (CRP). The cumulative effect of these alterations is an increase in inflammatory pathology and a decrease in protective immunity. The cumulative impact of hormone withdrawal is seen in the higher prevalence of elevated C-reactive protein and interleukin-6 in postmenopausal women in Nigerian cohorts when compared to males of the same age Heart disease, diabetes type 2, and osteoporosis are all more common in this group because of their inflammatory state [14].

4.2 Modified Innate Protective Reactions

Hormonal regulation has a profound effect on the first line of defence, the innate immune system. Neutrophils: Circulating neutrophil counts and the ratio of neutrophils to lymphocytes (NLR) are both elevated in menopausal women, suggesting an inflammatory condition. The association between this marker and the risk of hypertension and metabolic syndrome in postmenopausal women has been confirmed in studies conducted in Nigeria [10] Typically, oestrogen keeps macrophage activity in check. Its decrease enhances the production of IL-1 and TNF-α by macrophages, which in turn promotes tissue damage and chronic inflammation. During menopause, there is a dysregulation of NK cell cytotoxicity, even though progesterone normally downregulates NK function. Research has shown that alterations in NK function could make people more susceptible to hepatitis B and C viruses, which are common in Nigeria [4].

The ability of dendritic cells to deliver antigens and signal cytokines weakens adaptive immunological priming when oestrogen levels are low. Because of these intrinsic changes, older Nigerian women experience a higher infection burden and a delayed recovery rate.

4.3 Adaptive Loss of Immune Function

During menopause, a woman's adaptive immune system undergoes remarkable changes: As oestrogen levels drop, thymic involution speeds up, leading to a decrease in CD4+ helper and CD8+ cytotoxic T-cells. A study conducted by [7] found that HIV-positive women from Nigeria frequently experience a decline in the CD4/CD8 ratio. This change in the ratio is indicative of compromised immunological resistance and increased illness risk. In terms of B-cell activity, oestrogen improves both the survival rate and the synthesis of immunoglobulins. Vaccine responses (for viruses like influenza and hepatitis B) are diminished as menopause sets in because overall B-cell counts drop and antibody titers drop. It was found that compared to premenopausal controls, postmenopausal women in Nigeria had weaker seroconversion following hepatitis immunisation. During menopause, progesterone-induced regulatory T-cells (Tregs) decrease, which results in a decrease in immunological tolerance. Postmenopausal women may be more susceptible to autoimmune thyroiditis and systemic lupus erythematosus (SLE) due to this alteration. Rheumatology clinics in Nigeria have noticed that lupus flares in postmenopausal women are more severe than in women of childbearing age [19].

4.4 Enhanced Vulnerability to Contagious Illnesses

A woman's susceptibility to infections increases throughout menopause due to changes in her immune system. The hazards faced by women in Nigeria during menopause and perimenopause are heightened by endemic infections. ART-treated immunological reconstitution is less effective and CD4 declines more rapidly in postmenopausal HIV-positive women than in younger women. It was suggested that a decline in oestrogen levels could contribute to this worse prognosis. Malaria resistance decreases with age due to a decrease in immunity, and the disease is even more devastating when accompanied by anaemia. In areas of Nigeria where malaria is common, postmenopausal women have a higher risk of developing severe cases compared to younger adults [9]. Reactivation tuberculosis (TB) is more likely in women who are HIV co-infected because menopause-related immunosenescence reduces the integrity of granulomas. Recurrent urinary tract infections (UTIs) are a prevalent complaint among menopausal women in Nigeria. This is because decreased oestrogen thins the urogenital epithelium and changes the vaginal microbiota, making these infections more likely [12]

4.5 Menopause and Autoimmune Disorders

Loss of hormonal regulation makes women more likely to develop autoimmune illnesses, which is paradoxical given that total immune response reduces. By stimulating regulatory T cells (Tregs) and inflammatory cytokines, oestrogen and progesterone often keep tolerance in check. Their demise upsets this equilibrium and heightens autoreactivity. Menopause is associated with a worsening of autoimmune thyroid disorders, rheumatoid arthritis, and lupus in Nigeria [20]. One example is: Lesions are more severe and organ involvement is more common in menopausal women, which may be because Treg activity is reduced in this population. inflammatory indicators are higher and joint destruction is more aggressive in postmenopausal women compared to premenopausal women.

4.6 Immunoprevention and Vaccine Reactions

Hormonal state and age both affect the effectiveness of vaccines. The immunological responses to routine immunisations in women after menopause tend to be weaker. Hepatitis B vaccine results in lower incidence of seroconversion. Post-yellow fever vaccination antibody persistence is lower. An age-related decline in the efficacy of influenza vaccines in females [24] Because of this reduced reaction, postmenopausal women in Nigeria require individualised vaccination tactics, such as adjuvanted vaccines or booster doses.

4.7 Interactions Between the Brain and the Immune System

Additional modulation of immunity occurs after menopause as a result of psychological stress, which is prevalent owing to vasomotor symptoms, sleep difficulties, and cultural stigma. Increased levels of cortisol, a hormone associated with chronic stress, reduce the activity of lymphocytes and make the body more vulnerable to infections. Research out of Nigeria indicates that inflammatory markers and CD4+ count decreases are more pronounced in postmenopausal women who report higher levels of perceived stress [3]. This shows how crucial it is to include mental health in immunological treatment.

4.8 The Health Consequences in the Nigerian Context

Conditions during menopause in Nigerian women amplify immunological changes: HIV/AIDS, malaria, tuberculosis, and hepatitis are all very common. Iron, folate, vitamin D, and zinc deficiency all lower immunity. Low rates of immunisation and restricted availability of preventative healthcare. Social and cultural obstacles that make people reluctant to seek medical treatment Taken together, these considerations highlight the importance of investigating immunological health during menopause as a neglected yet crucial area of public health in Nigeria [25].

Conclusion

Important immunohaematological tipping points for women in Nigeria occur during menopause and perimenopause. Anaemia, coagulation problems, immunological suppression, an increased susceptibility to infections and autoimmune illnesses, and pro-inflammatory dominance are all symptoms of declining sex hormones. Nigeria is particularly vulnerable to these changes due to its inadequate laboratory infrastructure, high infectious illness load, and dietary inadequacies.

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