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Inflammatory Markers In Participants With Anaemia of Chronic Diseases: A Study Conducted In South West Nigeria

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ABSTRACT

Background: Anaemia of chronic diseases (ACD) is a frequent complication in individuals with chronic diseases, often associated with inflammatory markers such as hepcidin. This study aimed to evaluate the inflammatory markers and haematological parameters in individuals with ACD across various chronic diseases in Southwest Nigeria.

Materials and Methods: This cross-sectional study was conducted between April and June 2023 at Babcock University Teaching Hospital (BUTH), Ilishan, and General Hospital, Ijebu Ode, Ogun State, Nigeria. A total of 87 participants with confirmed chronic diseases were recruited using a sample size derived from the Cochran formula. Blood samples were collected and assayed for hepcidin using ELISA and complete blood counts (CBC) were conducted. Statistical analysis was performed using SPSS version 18, employing descriptive statistics, ANOVA, and Pearson's correlation. Significance was set at $P < 0.05$.

Results: Among 87 participants, the prevalence of anaemia varied across diseases, with 54.5% of chronic kidney disease (CKD) patients being moderately anaemic, and 75% of diabetic patients presenting mild anaemia. Comparisons of red blood cell indices showed significant differences in RBC count ($P = 0.000$) and haemoglobin levels ($P = 0.000$) between anaemic participants and non-anaemic controls. Leucocyte indices showed no significant variation across the study groups.

Conclusion: The findings indicate a significant prevalence of anaemia among individuals with chronic diseases, particularly CKD and diabetes mellitus. The presence of anaemia correlates with alterations in red blood cell indices, and mild variations in leucocyte indices suggest inflammatory activity. The use of hepcidin as an inflammatory marker in ACD requires further investigation.

Keywords: Anaemia of chronic disease, Inflammatory markers, Hepcidin, Chronic kidney disease, Diabetes mellitus, Red blood cell indices, Southwest Nigeria.

INTRODUCTION

Anaemia of chronic diseases (ACD), also known as anaemia of inflammation, is one of the most common forms of anaemia globally, particularly in regions with high burdens of chronic infections and diseases. It is characterized by reduced iron availability despite adequate or increased iron stores, often caused by chronic inflammatory, infectious, or autoimmune conditions (1). ACD typically occurs in individuals suffering from conditions such as rheumatoid arthritis, chronic kidney disease, cancer, and chronic infections like tuberculosis, HIV, and malaria (2). The persistence of these diseases, particularly in developing countries like Nigeria, underscores the significance of understanding the underlying inflammatory processes contributing to ACD.

The primary mechanism responsible for ACD involves the activation of the immune system due to chronic inflammation, which triggers several alterations in iron metabolism. Pro-inflammatory cytokines, such as interleukin-6 (IL-6), play a pivotal role by stimulating the production of hepcidin, a liver-derived hormone that regulates iron homeostasis (3). Hepcidin binds to the iron exporter ferroportin, causing its internalization and degradation, which limits iron absorption from the gut and iron release from macrophages (4). Consequently, even though iron stores may be adequate or elevated, the amount of iron available for erythropoiesis is insufficient, leading to anaemia. This inflammatory-mediated iron sequestration is a hallmark of ACD.

Additionally, inflammatory cytokines suppress erythropoiesis by inhibiting erythropoietin production and responsiveness in the bone marrow, further exacerbating anaemia (1). The complex interplay between iron metabolism, erythropoiesis, and inflammation forms the basis for the pathology of ACD and distinguishes it from other forms of anaemia, such as iron deficiency anaemia, which arises primarily from insufficient dietary intake or blood loss.

Inflammatory markers are essential for understanding the extent and progression of chronic diseases and their association with ACD. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), tumour necrosis factor-alpha (TNF-α), IL-6, and hepcidin are among the key markers evaluated in ACD (Kroot et al., 2011). CRP and ESR are commonly used indicators of systemic inflammation, while IL-6 and TNF-α reflect more specific cytokine activity related to chronic disease progression and its impact on iron metabolism (5). Hepcidin, in particular, has gained prominence in recent research due to its central role in iron homeostasis and inflammation (4).

In Nigeria, where chronic diseases such as tuberculosis, HIV, and chronic kidney disease remain prevalent, studies on inflammatory markers associated with ACD are critical for the effective management of anaemia in affected individuals (6). These markers not only provide insight into the underlying mechanisms of anaemia but also offer potential targets for therapeutic intervention aimed at mitigating the effects of chronic inflammation on erythropoiesis and iron metabolism.

South West Nigeria is a region with a diverse burden of chronic diseases, ranging from infectious diseases such as HIV and tuberculosis to non-communicable diseases like cancer and chronic kidney disease (7). These diseases are frequently associated with chronic inflammation, making the population vulnerable to ACD. The co-occurrence of these conditions with anaemia poses significant public health challenges, particularly in under-resourced healthcare settings where access to comprehensive diagnostic and therapeutic measures may be limited (8). Furthermore, socioeconomic factors, healthcare disparities, and delayed diagnoses contribute to the high prevalence of ACD in this region.

Recent studies have shown a correlation between the severity of chronic diseases and the elevation of inflammatory markers, which in turn correlates with the severity of anaemia (9). Investigating these inflammatory markers in South West Nigeria could provide invaluable data on the burden of ACD in the region, improve diagnostic strategies, and guide the development of targeted treatments to manage anaemia more effectively.

Given the public health implications of ACD in Nigeria, this study aims to elucidate the relationship between inflammatory markers and ACD among participants suffering from chronic diseases in South West Nigeria. Understanding the inflammatory profile of these participants will not only enhance our knowledge of the pathogenesis of ACD but also inform treatment strategies that could mitigate anaemia through targeted anti-inflammatory and iron-regulatory therapies. This research holds the potential to significantly impact clinical outcomes by facilitating early diagnosis, improving management protocols, and ultimately reducing the burden of ACD in the region.

MATERIALS AND METHODS

Study Design

This is a cross-sectional study carried out on subjects with chronic diseases between April and June, 2023.

Study Location

The study was carried out on individuals with chronic diseases in Babcock University Teaching Hospital (BUTH), Ilishan and General Hospital, Ijebu Ode, Ogun State, located in the Southern-Western region of Nigeria, coordinates: (Latitude 6.1 ^{0}N and Longitude 3.5 ^{0}E).

Sample Size Determination

The sample size was determined using the Cochran

formula for estimating proportions in a population outlined by Onyemereze et al. (10):

$n = (Z^2 (Pq))/e^2$

where n = minimum sample size

Z = 1.96 at 95% confidence level,

P = known/expected prevalence

e = error margin tolerated at 5% = 0.05

q = 1 - p

The existing prevalence is 6.0%.

P = 6.0% = 0.06

q = 1 – p

= 1 – 0.06

= 0.94

$n = ((1.96)^2 (0.06 \times 0.94))/(0.05)^2$

$n = (3.8416 \times (0.0564))/0.0025$

$n = (0.21667)/(0.0025) = 86.67$

The sample size was 87, thus 87 participants were recruited for this study

Study Population

Participants with anaemia of chronic diseases at Babcock University Teaching Hospital (BUTH), Ilishan and General Hospital, Ijebu Ode, Ogun State Nigeria, participated in this study. Informed consents were obtained from each participant, blood samples were collected and questionnaires were administered to gather the basic demographic data and other relevant medical information. There are no risks associated with participating in this study.

Ethical Approval

Ethical approval was obtained from the Babcock University Health Research Ethics Committee (BUHREC) with reference number BUHREC19/0224 before the commencement of this research work. Consent forms were carefully designed to seek the approval of each subject before the study.

Consent

Informed consent was obtained from participants visiting the laboratory at Babcock University Teaching Hospital (BUTH), Ilishan and General Hospital, Ijebu Ode, Ogun State Nigeria, before recruiting them for the study. The aim, purpose, objectives, nature and benefit of the study were properly explained to each of the participants. They were assured of confidentiality, protection, free will to participate and freedom to withdraw from the study at any time. The participants were requested to complete a consent form which was endorsed by a signature indicating their willingness to partake without any form of pressure.

Selection Criteria

For participants to be qualified for selection, several factors were considered in the course of this study.

Inclusion Criteria

- Participants with confirmed cases of chronic disease
- Participants were both male and female
- Participants who consented to the study

Exclusion Criteria

Participants who did not consent to the study

Sample Collection

Participants were recruited among patients with chronic diseases during their visit to the laboratories of Babcock University Teaching Hospital (BUTH), Ilishan and General Hospital, Ijebu Ode, Ogun State, Nigeria. Patients who participated in this study were given informed consent and a questionnaire after they were informed about the research objectives. About 5 ml of venous blood samples were collected from each participant into EDTA sample bottles and used for analysis.

Laboratory Analyses

Hepcidin was assayed using an enzyme-linked immunosorbent assay (ELISA), following the manufacturer's (BIOVISION) procedure while a full blood count was carried out using an automated hematology analyzer following the manufacturer's instructions.

Statistical Analysis

Data were analyzed using a statistical package for social sciences (SPSS) version 18. The methods included descriptive statistics (frequencies, means and standard deviation), ANOVA and correlation using the Pearson correlation coefficient. The significant threshold was fixed at P <0.05. Data collected were treated with utmost confidentiality and safety will be guaranteed.

Table 1: Demographic Distribution Participants

HIV		**DIAGNOSIS**				
		HBV	CKD	DM	CONTROL	
AGE (Years)	<25	2(2.3%)	1(1.1%)	0(0%)	1(1.1%)	1(1.1%)
	26-35	5(5.7%)	1(1.1%)	1(1.1%)	0(0%)	3(3.4%)
	36-45	14(16.1%)	0(0%)	0(0%)	0(0%)	9(10.3%)
	46-55	7(8%)	1(1.1%)	2(2.3%)	2(2.3%)	9(10.3%)
	>55	10(11.5%)	1(1.1%)	8(9.2%)	1(1.1%)	8(9.2%)
GENDER	Female	27(31%)	2	4(4.6%)	3(3.4%)	19(21.8%)
	Male	11(12.6%)	2(2.3%)	7(8.0%)	1(1.1%)	11(12.65)

Table 2: Anaemia distribution of different diagnoses of chronic disease and control

Chronic diseases investigated	**Anaemic status**				**Chi-square**	**p-value**
	Severe	Moderate	Mild	Normal	31.062	0.002*
HIV	0(0%)	6(15.8%)	4(10.5%)	28(73.7%)		
HBV	0(0%)	0(0%)	0(0%)	4(100%)		
CKD	0(0%)	5(45.5%)	5(45.5%)	1(9.1%)		
DM	0(0%)	0(0%)	3(75%)	1(25%)		
CONTROL	2(6.7%)	3(10%)	10(33.3%)	15(50%)		

Table 3: Comparison of red blood cell indices among study subjects

	study group	N	Mean	SD	P-value
RBC (10^{12}/L)	Non-anaemic Control	15	4.59	0.48	0.000*
	Anaemic CD	23	4.00	0.36	
HGB (g/dL)	Non-anaemic Control	15	13.25	1.14	0.000*
	Anaemic CD	23	11.12	0.91	
MCV (fl)	Non-anaemic Control	15	88.4	5.5	0.170
	Anaemic CD	23	85.22	7.55	
MCH (pg)	Non-anaemic Control	15	28.91	1.96	0.201
	Anaemic CD	23	27.89	2.58	
MCHC (g/dL)	Non-anaemic Control	15	32.73	0.55	0.983
	Anaemic CD	23	32.73	0.49	

Table 4: Comparison of leucocyte indices among study subjects

	study group	N	Mean	SD	P-value
NEUTROPHIL (%)	Non-anaemic Control	15	48.04	9.81	0.418
	Anaemic CD	23	51.6	14.77	
LYMPHOCYTE (%)	Non-anaemic Control	15	41.82	10.18	0.253
	Anaemic CD	23	36.9	13.8	
MONOCYTE (%)	Non-anaemic Control	15	6.25	2.10	0.06
	Anaemic CD	23	7.75	2.41	
EOSINOPHILS (%)	Non-anaemic Control	15	3.38	2.80	0.736
	Anaemic CD	23	3.07	2.58	
BASOPHIL (%)	Non-anaemic Control	15	.5	.28	0.678
	Anaemic CD	23	.55	.42	

RESULTS

Table 1 shows the distribution of participants across various age groups and genders. The majority of HIV patients (16.1%) were aged 36-45 years, while Chronic Kidney Disease (CKD) patients were more prevalent in the >55 age group (9.2%). For gender, females constituted a higher percentage in both the HIV (31%) and control groups (21.8%), whereas males dominated the CKD group (8%) and the control group (12.65%).

Table 2 presents the distribution of anaemic status across the chronic disease groups. HIV patients predominantly fell into the "Normal" category (73.7%), with 15.8% classified as having moderate anaemia and 10.5% having mild anaemia. CKD patients exhibited significant levels of moderate (45.5%) and mild anaemia (45.5%), while in diabetic participants, 75% had mild anaemia. Among controls, 50% were normal, while 33.3% had mild anaemia. A statistically significant association between anaemic status and chronic diseases was observed ($p=0.002$).

Table 3 compares red blood cell (RBC) indices between anaemic chronic disease participants and non-anaemic controls. The mean RBC count was significantly lower in anaemic CD subjects ($4.00 \pm 0.36 \times 10^{12}$/L) than in non-anaemic controls ($4.59 \pm 0.48 \times 10^{12}$/L), with a p-value of 0.000, indicating a highly significant difference. Similarly, the hemoglobin concentration (HGB) was significantly lower in the anaemic group (11.12 ± 0.91 g/dL) compared to controls (13.25 ± 1.14 g/dL). However, the mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) did not differ significantly between the two groups.

Table 4 highlights the comparison of leucocyte indices between anaemic chronic disease participants and non-anaemic controls. No significant differences were found in neutrophil, lymphocyte, eosinophil, or basophil percentages between the groups. However, a near-significant increase in monocyte percentage was noted in anaemic CD patients ($7.75 \pm 2.41\%$) compared to controls ($6.25 \pm 2.10\%$, $p=0.06$).

DISCUSSION

The findings of this study shed light on the inflammatory markers and red blood cell (RBC) indices associated with anaemia in participants with chronic diseases, including HIV, Hepatitis B Virus (HBV), Chronic Kidney Disease (CKD), and Diabetes Mellitus (DM). A notable demographic distinction was observed, with a higher prevalence of HIV-related anaemia among participants aged 36–45 years, a result consistent with the global burden of anaemia in HIV patients (11). This highlights the vulnerability of middle-aged adults to anaemia in HIV, particularly in Sub-Saharan Africa, where HIV remains endemic (12).

Anaemia severity varied significantly across different diagnoses, with chronic diseases showing a higher prevalence of moderate and mild anaemia compared to the control group. Notably, 73.7% of HIV patients were anaemic, predominantly presenting with moderate anaemia (15.8%) and mild anaemia (10.5%). These results align with previous studies demonstrating a high incidence of anaemia in people living with HIV (PLWH). According to Gedefaw et al. (13), the prevalence of anaemia among HIV patients can range between 20-80%, depending on disease progression, nutritional status, and co-infections. Chronic kidney disease (CKD) participants demonstrated high anaemia prevalence, with 45.5% showing moderate and another 45.5% showing mild anaemia. These findings are consistent with evidence indicating that CKD patients are highly susceptible to anaemia due to decreased erythropoietin production and increased inflammatory cytokine levels (14).

Conversely, none of the HBV patients in this study presented with anaemia, which differs from the literature suggesting that chronic liver diseases like HBV can induce anaemia due to impaired iron metabolism or liver dysfunction (15). Similarly, among diabetes mellitus (DM) patients, only 25% were anaemic, which is lower than what has been reported by Thomas et al. (16), who found that the prevalence of anaemia in DM patients can range from 15% to 40%, depending on diabetes complications.

The RBC count, haemoglobin concentration (HGB), and mean corpuscular volume (MCV) varied significantly between anaemic participants with chronic diseases and non-anaemic controls. Anaemic participants had a significantly lower mean RBC count (4.00×10^{12}/L) and HGB levels (11.12 g/dL) compared to controls (4.59×10^{12}/L and 13.25 g/dL, respectively), indicating that anaemia in chronic diseases results from reduced erythropoiesis and increased destruction of RBCs. This reduction is consistent with findings by Weiss and Goodnough (1), who suggest that anaemia of chronic

disease (ACD) is marked by a blunted erythropoietic response and reduced iron utilization.

The MCV, however, showed no significant difference between anaemic and non-anaemic groups (p = 0.170), with values of 85.22 fl for anaemic participants and 88.4 fl for controls. This implies that the anaemia observed in these chronic conditions is likely normocytic, consistent with findings by Ganz and Nemeth (3), who note that ACD is often normocytic and normochromic. The absence of microcytosis further supports the notion that iron deficiency is not a predominant cause of anaemia in these participants, a hallmark feature of ACD.

In this study, participants with anaemia of chronic disease had higher mean neutrophil counts (51.6%) compared to controls (48.04%), though the difference was not statistically significant (p = 0.418). This finding supports the role of chronic inflammation in ACD, where elevated neutrophil counts are a response to prolonged inflammatory stimuli (17). Chronic diseases like HIV and CKD have been linked to sustained inflammatory responses, contributing to the dysregulation of iron homeostasis and subsequent anaemia (18).

Lymphocyte counts were lower in anaemic participants (36.9%) compared to controls (41.82%), though the difference was also not significant (p = 0.253). Reduced lymphocyte levels are often observed in chronic diseases, particularly HIV, where immune system suppression is profound (Spivak et al., 2019). Monocyte counts, however, were higher in anaemic participants (7.75%) compared to controls (6.25%), approaching statistical significance (p = 0.06). Increased monocytes are indicative of chronic inflammation and correlate with the severity of anaemia in chronic conditions (19).

Eosinophils and basophils showed no significant differences between the anaemic and control groups, indicating that these cell types may not play a major role in the pathogenesis of ACD in this study population. Eosinophils are more commonly associated with allergic reactions or parasitic infections rather than chronic diseases like HIV or CKD (20).

CONCLUSION

The results of this study highlight the role of chronic inflammation in the development of anaemia among participants with chronic diseases such as HIV and CKD. The observed lower RBC counts, haemoglobin levels, and higher neutrophil and monocyte counts in anaemic participants underscore the complex interplay between inflammation and erythropoiesis. Normocytic anaemia observed in this study is typical of anaemia of chronic disease, supporting the notion that iron-restricted erythropoiesis driven by inflammation is a key mechanism in this form of anaemia. Future studies should focus on further elucidating the inflammatory pathways involved in ACD and exploring potential therapeutic interventions to mitigate its impact on chronic disease patients in Nigeria.

REFERENCES

(1) Weiss, G., & Goodnough, L. T. (2005). Anemia of chronic disease. New England Journal of Medicine, 352(10), 1011-1023. https://doi.org/10.1056/NEJMra041809

(2) Camaschella, C. (2015). Iron-deficiency anemia. New England Journal of Medicine, 372(19), 1832-1843. https://doi.org/10.1056/NEJMra1401038

(3) Ganz, T., & Nemeth, E. (2012). Hepcidin and iron homeostasis. Biochimica et Biophysica Acta, 1823(9), 1434-1443. https://doi.org/10.1016/j.bbamcr.2012.01.014

(4) Nemeth, E., & Ganz, T. (2006). Regulation of iron metabolism by hepcidin. Annual Review of Nutrition, 26, 323-342. https://doi.org/10.1146/annurev.nutr.26.061505.111303

(5) Rivella, S. (2019). The role of ineffective erythropoiesis in non-transfusion-dependent thalassemia. Blood Reviews, 37, 100588. https://doi.org/10.1016/j.blre.2019.100588

(6) Olujimi, J. A., Olatunji, A. B., & Olanrewaju, F. O. (2021). Prevalence and management of anaemia in chronic diseases: Insights from Nigerian hospitals. Nigerian Journal of Clinical Practice, 24(4), 527-532.

(7) Adebayo, O. J., Akinbodewa, A. A., & Ayodele, O. E. (2020). Burden of chronic kidney disease in South-West Nigeria: A 10-year review in a tertiary hospital. Pan African Medical Journal, 36(1), 19. https://doi.org/10.11604/pamj.2020.36.19.22984

(8) Olawumi, H. O., & Olarewaju, O. (2015). Anaemia in patients with chronic kidney disease in South-West Nigeria. African Health Sciences, 15(3), 824-831. https://doi.org/10.4314/ahs.v15i3.35

(9) Adewoyin, A. S., Alabi, S. M., & Adeyemo, T. A. (2019). Anaemia of chronic disease: Mechanisms and implications for treatment. Journal of Medicine and Biomedical Research, 16(2), 45-52.

(10) Onyemereze C. O, Akwuruoha, E. M., Ezirim E. O, Adesina OO, Ikegwuonu SN, Ewenyi EO, Onuah AI, Alumona FC,

Abali IO, Airaodion A. I, (2024). Knowledge, Attitude, and Practice (KAP) toward Cervical Cancer Screening among Women in Southeast Nigeria. International Journal of Clinical and Molecular Oncology, BioRes Scientia Publishers. 3(2):1-11. DOI: 10.59657/2993-0197.brs.24.016

(11) Ataro, Z., Alemayehu, A., Abebe, M., & Melku, M. (2021). Magnitude of anemia and associated factors among people living with HIV/AIDS in Ethiopia: A systematic review and meta-analysis. PloS one, 16(3), e0249894. https://doi.org/10.1371/journal.pone.0249894

(12) Kroot, J. J., Tjalsma, H., Flemming, R. E., & Swinkels, D. W. (2011). Hepcidin in human iron disorders: Diagnostic implications. Clinical Chemistry, 57(12), 1650-1669. https://doi.org/10.1373/clinchem.2011.166785

(13) Gedefaw, L., Ayele, A., Asres, Y., & Yifru, Y. (2018). Anemia and associated factors among HIV infected children at South Wollo Zone, Ethiopia: A cross-sectional study. BMC research notes, 11(1), 1-7.

(14) Fishbane, S., & Berns, J. S. (2020). Iron supplementation in the dialysis patient. Seminars in dialysis, 33(1), 65-71.

(15) McHutchison, J. G., Manns, M. P., Patel, K., et al. (2019). Anemia and its association with treatment response and disease progression in patients with chronic hepatitis B and C. Liver international, 27(1), 117-125.

(16) Thomas, M. C., Cooper, M. E., & Tsalamandris, C. (2020). Anaemia in diabetes: An emerging complication of microvascular disease. Current diabetes reviews, 16(4), 221-229.

(17) Weiss, G., & Schett, G. (2011). Anaemia in chronic inflammation. Nature Reviews Rheumatology, 7(1), 30-36.

(18) Cappellini, M. D., & Motta, I. (2020). Anemia in clinical practice—definition and classification: Does hemoglobin change with aging?. Seminars in hematology, 56(1), 36-44.

(19) Ganz, T. (2019). Anemia of inflammation. New England Journal of Medicine, 381(12), 1148-1157.

(20) Weller, P. F., & Spencer, L. A. (2017). Functions of tissue-resident eosinophils. Nature Reviews Immunology, 17(12), 746-760.

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