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Research Article *Open Access*

Anaemia: A New Modifiable Risk factor among People Living With Dementia in Uganda

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Abstract

Background: Anaemia describes a condition in which there is a reduction of haemoglobin concentration in the blood of an individual to a level below 11g/dl. Anaemia is very common after age 65 years, accounting for 4.2% to 28 when WHO criteria are applied in different gender and age groups. Dementia is a clinical syndrome that affects memory, thinking, behaviour and ability to perform everyday activity. Dementia is a growing public health problem and results in cognitive decline and behavioural problems that lead to impairment in activities of daily living. WHO in 2021 reported that more than 50 million people were living with dementia, and about 10 million new cases are detected every year. There is a paucity of data in the area of dementia research from Sub-Saharan Africa and Uganda. Many patients are undiagnosed clinically due to non-consideration of readily accessible laboratory blood biomarkers. The current study was performed on people lining with dementia attending Hospitals in Kampala, Uganda to assess and compare levels of erythrocytes, leucocytes and platelets with non-demented control group Using Haematological biomarkers may be useful in dementia diagnosis.

Objective of the study: A case-control study was conducted to assess some Haematological profile as possible diagnostic biomarkers of Anaemia among Dementia patients attending five selected referral Hospitals in Uganda.

Methods: A case-control study was conducted among patients presenting consecutively to the Neurology and Psychiatric clinics of Mulago National Referral Hospital (MNRH).Kampala,Uganda and Kiruddu National Referral Hospital (KNRH) Kampala,Uganda between January to December, 2024. Seventy-eight (78) elderly patients aged fifty years and older diagnosed with dementia by a Specialist or Medical Officer were recruited as case subjects while Seventy-eight (78) cohort subjects age and sex matched with no history of dementia served as control. Social demographics, clinical and laboratory characteristics were assessed for both cases and controls. Questionnaires with close-ended questions and Dementia diagnostic tools (MMSE)and Blessed Dementia Scale (BDS) were distributed to participants to collect data. Ten millilitres (10 ml) of blood samples were collected aseptically from antecubital vein from participants into Sodium EDTA vacutainer bottles for assessment of Haematological parameters using Mindray autoanalyzer for Complete Blood Count (CBC) analysis. Quantitative data was collected and

entered into a Microsoft excel spreadsheet and exported into STATA software version 14.0 for analysis. Descriptive statistics including frequencies, percentages, mean and standard deviation were used to describe the Social demographics of the cases and controls. P-values of <0.05 was chosen to be statistically significant.Fisher's exact test and odd ratios were used to establish association of parameters with dementia. Confounders were ruled out by performing post-diagnostic checks like VIF (Variance Inflation Factors) to ensure that those that are highly collinear are eliminated.Ethical approvals were obtained from Mount Kenya University Ethical Review Committee (MKU/ISERC/3354) and St. Francis Hospital Research Ethics Committee (SFREC-2023-117).

Results: The findings in the present study revealed statistically significant differences ($p<0.05$) and very low values in the means of Haemoglobin concentration, RBC count, Haematocrit, MCV,MCH, MCHC, and RDW-SD when the case group was compared with the control group.

Conclusion: Based on the result obtained, decreased erythrocytes and RBC indices may be possibly involved in the pathogenesis of dementia.

Keywords: Dementia**,** Erythrocytes, Haemoglobin, Haematocrit, Mean Cell Volume.

INTRODUCTION

The current study was performed on people living with dementia attending Hospitals in Kampala, Uganda to assess and compare levels of erythrocytes and red cells indices of dementia subjects with non-demented control group.

Anaemia is defined by World Health Organization as a condition in which the number of red blood cells or the haemoglobin concentration within them is lower than normal (WHO,2025) There is a reduction of haemoglobin (Hb) concentration in the blood of an individual to a level below 11g/dl. Anaemia is a public health concern that affect majorly young children and pregnant women in resource-poor countries (WHO,2001). Anaemia is very common in after age 65 years, accounting for 4.2% (Nilsson -Ehla *et al*.,2000) to 28% (Atti et al.,2006) when WHO criteria are applied in different gender and age group. Anaemia has consequences for human health as well as social and economic development.

For older persons the criteria for anaemia may not be as widely accepted as for younger people. The haemoglobin concentration is lower on average in people of older age and could therefore necessitate an adjustment of the criteria set by WHO. On the other hand, the decline in haemoglobin concentration during aging is small and may not require unique criteria. (Nilsson -Ehla *et al*.,2000). Although cross-sectional studies found an association between anaemia and dementia longitudinal studies provided contradictory results(Atti et al.,2006) Anaemia is one of the most common nutritional deficiency diseases observed globally and affects more than a quarter of the world's population (WHO/CDC, 2018). Anaemia affects 1.62 billion people (25%) globally, whereby 56 million are elderly (Atti et al.,2006) Currently, there is limited local data on laboratory specific studies and factors associated with anaemia in dementia in Uganda.

The hemoglobin test results were categorized into mild, moderate, and severe anaemia based on WHO guidelines: Mild anaemia: Hemoglobin levels between 10.0–10.9 g/dL Moderate anemia: Hemoglobin levels between 7.0–9.9 g/dL and Severe anemia: Hemoglobin levels below 7.0 g/dL. WHO defined Dementia as a group of disorders characterized by a decline from a previously attained cognitive level that affects activities of daily living and social functioning (WHO,2023)

Dementia is a clinical syndrome that affects memory, thinking, behaviour and ability to perform everyday activity. (Alzheimer's Association,2023;WHO,2023) Dementia is a growing public health problem and results in cognitive decline and behavioural problems that lead to impairment in activities of daily living. WHO in 2021 reported that more than 50 million people were living with dementia, and about 10 million new cases are detected every year.

WHO defined Dementia as a group of disorders characterized by a decline from a previously attained cognitive level that affects activities of daily living and social functioning (WHO,2023). Among many causes of dementia are hypothyroidism, chronic alcohol abuse, brain tumours,subdural hematomas, psychiatric depression, traumatic brain injury, infections (HIV and Syphilis), vitamin deficiencies, cardiovascular diseases and chemotherapy related cognitive dysfunction(Khalil *et al*,2021)

Various disorders impact memory, cognition, behaviour, and daily activities; they are together known as dementia (WHO,, 2023). Memory and language are two of the cognitive areas that suffer reductions, leading to diminished functioning; nonetheless, awareness, alertness, and attention is unaffected. (Oh and Rabins, 2019).Very elderly people may show dementia symptoms which include losing tract of time, forgetting recent events, difficulty in solving problems or making decision, it is not part of normal ageing (Fynat,2018). Llibre-Rodríguezes et al. 2017, reported that disability, dependency and other abnormalities seen among older people in Latin America, are majorly caused by dementia.

Dementia affects an estimated 55 million individuals globally, with the World Health Organization reports that around 10

million new cases are diagnosed annually. (WHO, 2023) projections. The increasing incidence of chronic illnesses and the aging population are projected to cause a substantial rise in the burden of dementia in Low-Middle income countries.(LMICs) across the African, Asian, and Latin American continents (UNDESA, 2015)

Approximately 5-8 percent of the global population aged 60 and up is affected by dementia. An estimated 2.13 million individuals in Sub-Saharan Africa were impacted by dementia in 2015, according to 2019 research by Kehoua et al. (2019) With the greatest expected growth in Eastern and Central Sub-Saharan Africa, the research predicted that the number would reach 3.38 million as of 2030 and 7.26 million as of 2050 (Kehoua et al., 2019). After cancer (2.0%), musculoskeletal illnesses (8.9%), cardiovascular diseases (5.0%), and cerebrovascular diseases (5.0%), dementia takes up the lion's share percentage of disability-adjusted life years (DALYs) for those aged 60 and above (9.5%) (Fymat, 2019).

With the rapid rise in population growth and increase in the population, dementia is on the rise among the elderly and together with other non-communicable diseases, this portends a great economic burden. Dementia is perceived as part of normal aging in Africa, therefore many people living with dementia are suffering undiagnosed or diagnosed very late due to lack of awareness. Many cardiovascular risk factors and oxidative stress have been attributed to causing Dementia. (Butterfield and Halliwell, 2019; He *et al.*, 2020). Clinical utility have been found in Haematology parameters in patient living with demmtia in studies conducted by Akingbade *et al.*,2018; Khalil *et al*,2021 and Schrolder *et a*l,2022,

Using the clinical practice management guideline for dementia, Shaji *et al.*, 2018, gave the following tests used in clinical practice management to assess or exclude dementia: Complete/ Full Blood Count (CBC/FBC), Lipid Profile tests, Erythrocyte Sedimentation Rates (ESR) , liver, renal and thyroid function Tests, hormonal assay, serum level of urea, electrolytes, urine analysis, VDRL / TPHA, HIV, Calcium, Vitamin B12, phosphate and folic acid assay (Shaji *et al.*, 2018).

Available findings from multiple studies show that there is a need to further study blood biomarkers of relevance to dementia in Ugandan hospital setting (Ahmed *et al.*, 2014., Kamoga *et al.*, 2019; Lekoubou *et al.*, 2014).

Musisi *et al.*,2008) Nakasujja *et al.*, 2007 and Namuli,2015) reported that data on studies conducted on dementia in Uganda were limited and there were needs to carry out more research in this area. This present study therefore assessed some haematological parameters of potential relevance to people living with dementia in Uganda.

OBJECTIVE OF THE STUDY

This study was conducted to determine association of anaemia with dementia using haematological profile of patients attending elected referral Hospitals in Kampala,Uganda

Hypotheses

Objectives - H_1: Alternative /Research Hypothesis

There is a significant (positive or negative) association between anaemia and dementia.

H_0: Null Hypothesis

There is no association between anaemia and dementia

METHOD

Materials and Equipment

Mindray Haematology Autoanalyzer, Table top high-speed haematocrit centrifuge (Max Speed = 16000 rev/min); Refrigerator, Freezer, Syringes and needles, cotton wool, gloves, blood vacutainer bottles, test tubes, Potassium EDTA anticoagulant bottles, Haematology auto-analyser reagents, 70% alcohol swab.

Study Design, Setting and Population

A case-control study was conducted to assess some Haematological parameters as possible diagnostic biomarkers of anaemia among Dementia patients attending Mulago and Kiruddu National Referral Hospitals, Kampala between January and December.2024. Dementia cases were selected from the population of people living with dementia undergoing treatment at the Psychiatric and Neurology clinics of Mulago and Kiruddu National Referral Hospitals. Participants for the control group were selected from three different hospitals in Kampala, Uganda. These are Lubaga, Mengo, and Nsambya Hospitals.

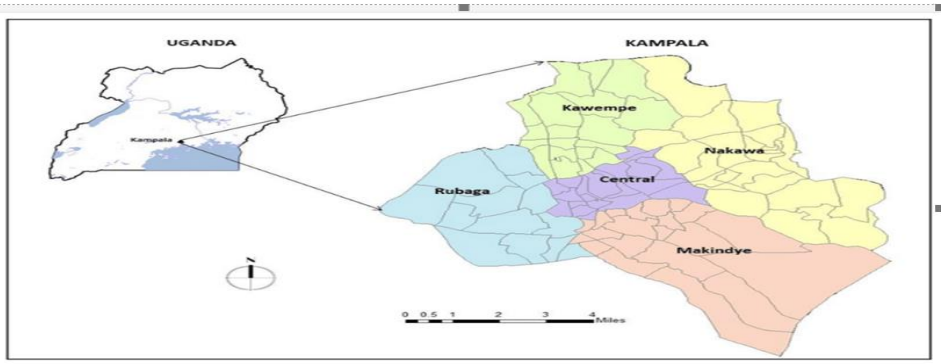


Figure 1: Showing Map of Study area where the research was conducted in Kampala, Uganda.

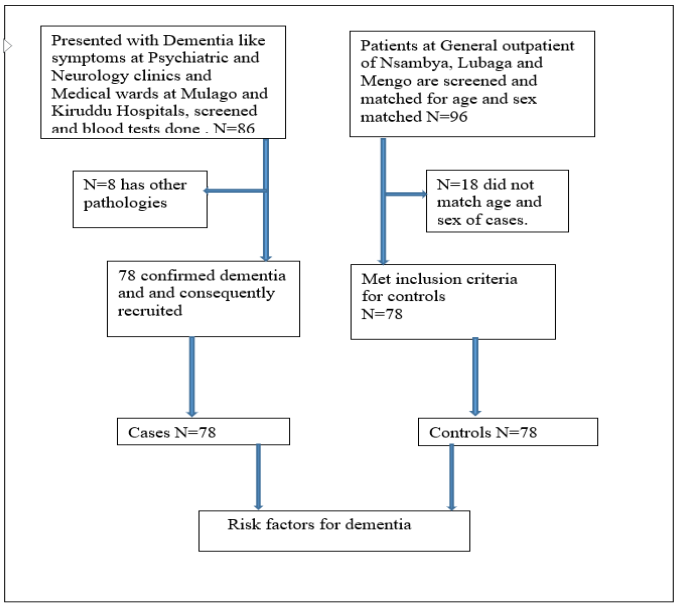


Figure 2: Flow diagram for participant's selection

Participants were people living with dementia who visited the research locations (Mulago, Kiruddu, Lubaga, Mengo and Nsambya Hospitals) during the study period (January,2024-December,2024) and who fulfilled all inclusion criteria.

Study Population

All Ugandans afflicted with dementia who visited the research locations (Mulago, Kiruddu, Lubaga, Mengo and Nsambya Hospitals) during the study period January, 2024-December, 2024) and who fulfilled all inclusion criteria.

Eligibility Criteria

Inclusion Criteria

Clinical diagnostic and cognitive testing for dementia measured by Mini Menta State Examination (MMSE) and screened by Blessed Dementia Scale (BDS)

- Participants 50 years and older
- Hospital based participants
- Deterioration of memory and other mental capacities throughout time.
- No disturbance of awareness and consciousness occurs.

Exclusion Criteria

The research excluded: participants, hospital based, 50 years and above who declined to participate.

Sample size determination for Case-Control study

Armitage, Berry, and Mathew (2008) presented a method for determining the sample size of comparison groups. In particular, the researcher determined dementia patient sample size using this formula:

$$n = \frac{Z^2 pq}{d^2}$$

Sample size = n

Z= standard normal deviation, generally 1.96 (95% confidence level).

Value at 95% confidence interval (1.96)

p=Local prevalence of condition (5% or 0.05) (WHO,2019)

q=1-p, the desired confidence level

d=Error margin (5% or 0.05) or Level of accuracy

Therefore, $n = \frac{1.96^2 \times 0.05 \times 0.95}{0.0025}$

$n = \frac{3.84 \times 0.05 \times 0.95}{0.0025}$

$n = \frac{0.182476}{0.0025}$

$n = 72.99 = \mathbf{73}$

78 participants were selected as cases to cater for attrition and loss to follow up and 78 age and sex matched control group was also selected.

Type of test: **two-sided test**

Experimental and Techniques

Sampling Procedure and testing

Blood samples of dementia patients were collected from Mulago and Kiruddu Hospitals. Venous blood samples of the dementia and control group were collected aseptically by the researcher using graduated syringes of 10ml. This blood was distributed into Sodium EDTA anticoagulant vacutainer bottles; which was analyzed for levels of erythrocytes, leucocytes and platelets through the Complete Blood Count (CBC) test. The EDTA samples which had whole blood were analyzed immediately. The analysis was carried out at Makerere University Biochemistry Laboratories, Kampala,Uganda and Islamic University Medical Centre Laboratory using Mindray Haematology Analyzer.The parameters in included in Complete Blood Count (CBC) are: Haematocrit,Red Blood Cells(RBC) Count, White Blood Cells(WBC) MCV,MCH,MCHC, Platelets, Mean Platelet Volume, Platelet Distribution Width, Haemoglobin, Absolute and differential Neutrophil count Absolute and differential MID (Eosinophil Basophil and Monocytes) and Absolute and differentia Lymphocytes .The tests with outrageous values or outliers were repeated for the reliability of results and quality control.

Data Collection and Analysis

Social demographic data was collected for information on age, sex, marital status , residence, religion affiliation .The descriptive statistics including frequencies, mean values, minimum and maximum values were analyzed using STATA version 14.0.Each parameter of CBC in the cases and control groups were compared with normal range.Fishers Exact test and Odd ratios were carried out to establish association of social demographic characteristics and biomarkers with dementia.

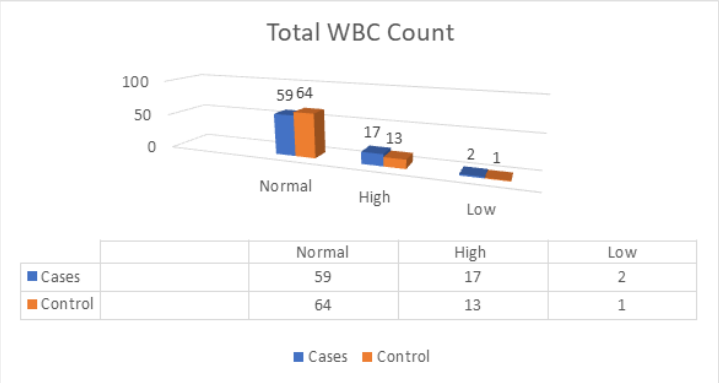
Statistical Analysis

A t-test was applied to see the significance of difference between dementia patient group with the control group. For each CBC parameter, p-value of less than 0.05($p<0.005$) was considered the significant.

RESULTS

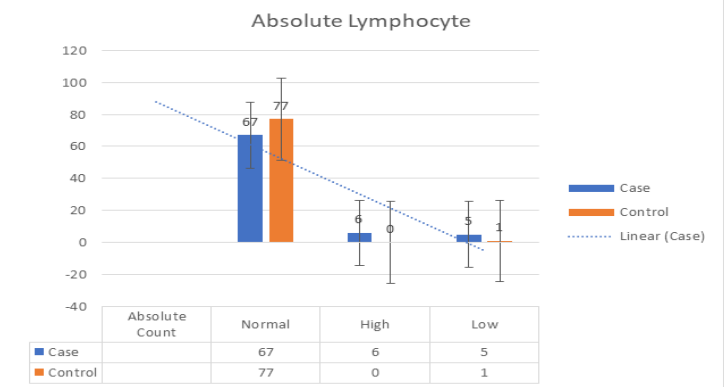
Association of Haematological parameters with dementia

The objective of this study is to determine the association of HHaematological parameters (Haemoglobin, Haematocrit, Platelets, White blood cell count, MCV, MCH, MCHC) with dementia among people living with dementia in selected referral hospitals in Uganda (Case-control study).



		Normal	High	Low
Cases		59	17	2
Control		64	13	1

Figure 3.1 showing association of Total WBC with Dementia



Absolute Count	Normal	High	Low
Case	67	6	5
Control	77	0	1

Figure 3.2 showing association of Absolute Lymphocytes with Dementia

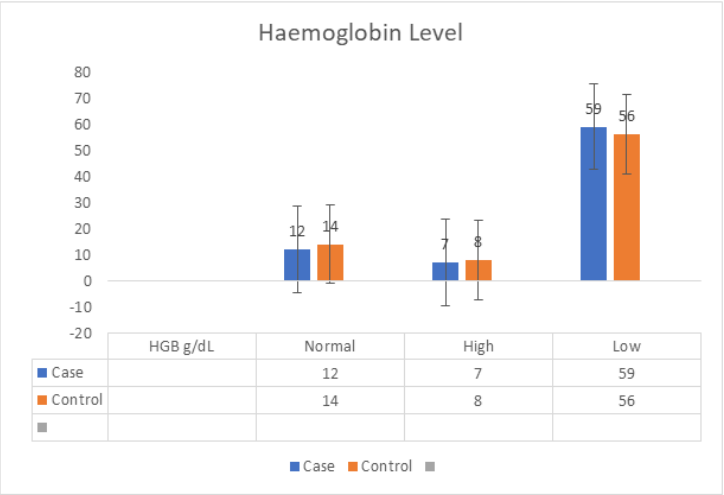


Figure 3.4 showing association of Haemoglobin level with Dementia

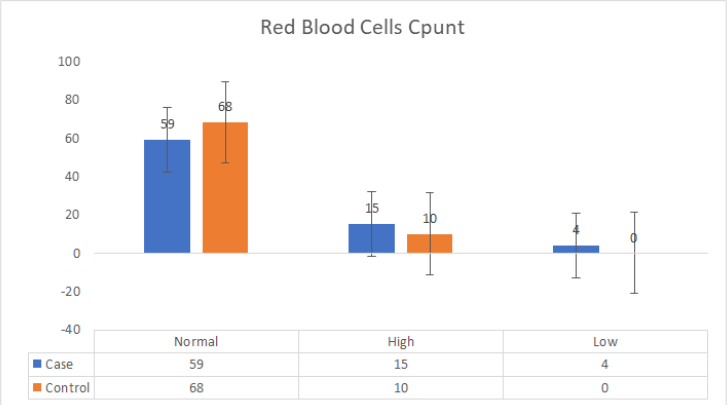


Figure 3.5 showing association of Red Blood Cells level with Dementia

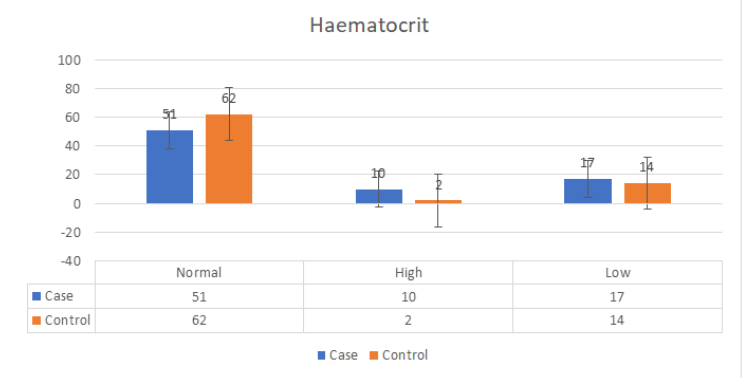


Figure 3.6 showing association of Haematocrit level with Dementia

Table 3.1: Logistic regression output

Variable	Category	Estimate	Std. Error	p-value
(Intercept)		17.59	0.10	0.00
Lymphocytes	Low	35.09	0.69	0.00
	Normal	16.69	0.27	0.00
Granulocytes	Low	0.02	0.39	0.00
	Normal	16.69	0.27	0.00
Lymphocyte Percent	Low	33.65	0.22	0.00
	Normal	0.04	0.62	0.00

Gran_Lymph_Ratio	Low	0.51	0.95	0.00
	Normal	1.46	0.95	0.00
Deviance statistics	Min	IQ	Median	Max
	-1.35	-0.95	0.00	1.43
Model Fit statistics	Null deviance	Residual deviance		
	216.26 (df = 155)	185.29 (df = 147)		

Interpretation

From the results above, patients with low lymphocytes were 35 times more likely to report dementia compared to their counterparts who had high lymphocytes values. Similarly, those whose lymphocytes are categorized as normal, were 16 times less likely to report dementia compared to their counterparts with high lymphocytes. The data further indicates that those with low granulocytes were less likely to report dementia compared to those with high count of granulocytes.

Social Demographic characteristics of the participants

Table 3.2: showing association of Socio-demographics with Dementia

Parameter	Category	Count (%)	Case	Control	P-Value
Gender	Male	78(50)	48.5%	49.0%	**P>0.05**
	Female	78)50)	51.5%	51%	
Age Distribution	50 - 59 years	54(35)	62.9%	37.1%	P>0.05
	60 - 69 years	50(32)	63.0%	37.0%	
	70 - 79 years	39(25)	59.0%	41.0%	
	80 - 89 years	10(6)	40.0%	60.0%	
	90 years and above	3 (2)	0.0%	100.0%	
Education	Non formal	26(17)	69.2%	30.8%	**P<0.001***
	Primary	67(44)	72.2%	27.8%	
	Secondary	35(22)	57.1%	42.9%	
	Tertiary	28(18)	17.9%	82.1%	
Marital Status	Single	8(5).	50%	50%	P>0.05
	Married	65(42)	62%	38%	
	Separated	32(21)	66%	34%	
	Widowed	47(30)	51%	49%	
	Divorced	4(2)	75%	25%	
Religion	Muslim	26 (17)	69%	31%	P>0.05
	Pentecostal	5 (3)	100%	0%	
	Catholic	71 (46)	61%	39%	
	Protestant	40 (26)	48%	53%	
	Others	14(9)	50%	50%	
Residence	Rural	57 (37)	56%	44%	P>0.05
	Slum	2(1)	100%	0%	
	Urban	97(62)	61%	39%	
Living with relatives/Family	No	80(51)	90%	10%	**P<0.001***
	Yes	76(49)	40%		

DISCUSSION

Haematological biomarkers were analyzed using three (3) parts Mindray Haematology Auto-Analyzer. For erythrocyte count and red cell indices, the current study revealed a significant reduction in Red Blood Cell (RBC) Count, Haemoglobin (HBG) concentration, Haematocrit (HCT) percentage, values of MCV, MCH, MCHC and significant increase in RDW-SD but the increase in RDW-CV is not significant in dementia group compared to the control significant decrease in Red Blood Cells (RBC) Count, when the dementia case group is compared with the control group.This finding indicate the presence of Anaemia in the dementia patients. The low values observed in Haematocrit, RBC, Haemoglobin, MCV, MCH, MCHC in the dementia group may explain lack of oxygen and nutrient to the brain thereby causing dementia. This finding in the erythrocytes might be due to changes in haematological indices especially related to RBCs. These findings further agree with the report given from the study conducted by Khalil *et al*,2021 in South Punjab, Pakistan among dementia patients. They reported that the mean value for every erythrocyte was lower than the normal range. A significant difference existed for each erythrocyte between dementia group and controls except MCHC. This observation of low erythrocyte value may likely hamper microcirculation in the cerebral tissues leading to micro-infarcts or microbleeds which cause neuronal insults and parenchymal damage. However, there was low levels obtained for Neutrophils and in contrast to the finding in this study. The value obtained by Khalil *et al*,2021 for total

WBC was significant whereas our finding showed the contrary when they stated that significant differences existed in the WBC levels between controls and PD patients. However, the WBC level in our finding was not significantly different between dementia patients and control group. The results of the present study also demonstrated significantly lower percentage values for Haematocrit (HCT) and Haemoglobin (HB) concentration in dementia groups compared to the control. This result is in accordance with the reports of findings of Hong *et al*.,2020 in their Nationwide , population based cohort study conducted in Taiwan; Atti *et al*.,2006 who carried out a longitudinal population study on ageing and dementia in Stockholm, Sweden) who reported a significantly positive correlation between anaemia and dementia. The implication of this finding is that the resulting anaemia due to low erythrocytes and RBC indices might increase the risk of dementia because of chronic brain hypo-oxygenation (Atti *et al*.,2006; Hong *et al*.,2020; Weiss *et al*.,2022)

CONCLUSION

Based on the results obtained, from the current study, decreased erythrocytes and RBC indices (Anaemia) , surge in leucocyte and platelets count may be possibly involved in the pathogenesis of dementia.

6.0 Acknowledgement

We acknowledge the patients from the participating Hospitals who gave us consent to obtain this information and allowed us to collect their blood samples.

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Conflict of Interest Statement

Authors declare that they have no actual or potential conflicts of interest or competing interest

Additional Information

Ethical Approval: The study conformed to ethical review board requirements and got approvals from Mount Kenya University Ethical Review Committee (MKU/ISERC/3354) and St. Francis Hospital Research Ethics Committee (SFREC-2023-117)

Human Subjects: Consent was obtained from all patients and participants in this study

Financial relationship: The authors declare that they have no financial relationships at present or within the previous three years with any organization that might have an interest in the submitted work

Other Relationships: The authors declare that they have no other or activities that could appear to have influenced the submitted work relationships at present or within the previous three years with any organization that might have an interest in the submitted work

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