SAR Journal of Anatomy and Physiology

Abbreviated Key Title: *SAR J Anat Physiol*
Home page: https://sarpublication.com/journal/sarjap/home
DOI: https://doi.org/10.36346/sarjap.2025.v06i01.001

OPEN ACCESS

ISSN 2707-7713 (P)
ISSN 2709-6874 (O)

Original Research Article

Studies on C-Reactive Protein, Erythrocyte Sedimentation Rate, White Blood Cell and Differential White Cell Counts in Patients Diagnosed with Rheumatoid Arthritis in Owerri, Nigeria

Aloy-Amadi Oluchi C[1*], Umah Valentine C[1], Emeka-Obi Obioma R[2], Akogu Okechukwu[3], Ezeh Caleb C[4], Johnkennedy Nnodim[1]

[1]Department of Medical Laboratory Science, Imo State University, Owerri, Nigeria
[2]Department of Haematology, College of Medicine, Federal University of Technology, Owerri, Nigeria
[3]Department of Optometry, Imo State University, Owerri, Nigeria
[4]Department of Haematology, Federal Teaching Hospital, Owerri, Nigeria

***Corresponding Author:** Aloy-Amadi Oluchi C
Department of Medical Laboratory Science, Imo State University, Owerri, Nigeria

Article History: | Received: 15.12.2024 | Accepted: 21.01.2025 | Published: 23.01.2025 |

Abstract: ***Background*:** Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease characterized by persistent synovial inflammation, joint pain, and progressive joint damage. It affects approximately 1% of the global population, disproportionately impacts women and is associated with significant morbidity, reduced quality of life, and economic burden. ***Aim*:** This study was aimed at determining the changes in some haematological parameters and C-reactive protein in rheumatoid arthritis patients attending Federal University Teaching Hospital, Owerri, Imo State, Nigeria. ***Methods*:** A cross-sectional study was carried out from the month of June to August, 2023, and all subjects who gave a written informed consent were enrolled in the study. The study population consisted of 50 rheumatoid arthritis and an equivalent number of age matched apparently healthy patients who served as controls. The procedure was carried out at the Federal University Teaching Hospital, Owerri, and standard operating procedures were followed. The results of the tests were analyzed using SPSS version 21. Eight millilitres of venous blood sample was collected at the ante-cubital vein aseptically, 4ml was dispensed into ethylenediaminetetraacetic acid containers for the estimations of erythrocyte sedimentation rate (ESR), white blood cell (WBC) and differential white cell counts, while the remaining 4ml was dispensed into plain containers for the determination of C-Reactive Proteins. The EDTA and plain containers were properly labeled with the subject's name, sample number and date of collection. The blood sample dispensed into the EDTA containers were stored in a refrigerator at 4^0C while the serum was stored in a freezer at -20^0C prior to use. ***Results*:** The mean values of TWBC, (15.04 ± 13.98) cells/µl, neutrophils (62.67 ± 16.08) %, eosinophils (5.47 ± 3.39)%, and monocytes (4.70 ± 3.12)% were significantly raised in rheumatoid arthritis patients when compared to controls (8.93 ± 2.35) cells/µl, (51.52 ± 10.79)%, (28.07 ± 10.12)%, (3.28 ± 2.54)% and (1.80±1.29)% (p = 0.031, p= 0.000, p= 0.001, p= 0.002 and p=0.000). The mean values of lymphocytes (28.07 ± 10.12) %, was significantly reduced in rheumatoid arthritis patients when compared to controls (40.48±10.92) %. The mean value of ESR (50.16 ± 40.87) mm/hr and C-reactive protein (79.16 ± 55.55) mg/dl were significantly increased in rheumatoid arthritis patients when compared to controls (6.89 ± 2.09) mm/hr and (8.32 ± 3.03) mg/dl respectively (p= 0.000 and p=0.001). There were no significant differences in the mean values of WBC, neutrophils, lymphocytes, eosinophils, monocytes, ESR and C-reactive protein in male rheumatoid arthritis compared to female rheumatoid arthritis patients (p=0.886, p=0.695, p=0.881, p=0.652, p=0.341, p=0.516 and p=0.434). A significant positive correlation of C-reactive protein occurred with ESR, WBC and neutrophils in rheumatoid arthritis patients (r=0.32, p=0.011, r=0.44 and p=0.021, r=0.54, p=0.043), and a non-significant positive correlation with lymphocytes, monocytes and eosinophils (r=0.87, p=0.179, r=0.96, p=0.317 and r=1.06, p=0.398). ***Conclusion*:** Rheumatoid arthritis is associated with increase in total white blood cell, neutrophils, eosinophils, monocytes counts, ESR and C-reactive protein. Lymphocytopenia is linked to rheumatoid arthritis. Therefore, monitoring the parameters in rheumatoid arthritis is essential for diagnosis, disease activity assessment, and management.

Keywords: C-Reactive Protein, Erythrocyte Sedimentation Rate, White Blood Cell, Differential White cells, Rheumatoid Arthritis.

Citation: Aloy-Amadi Oluchi C, Umah Valentine C, Emeka-Obi Obioma R, Akogu Okechukwu, Ezeh Caleb C, Johnkennedy Nnodim (2025). Studies on C-Reactive Protein, Erythrocyte Sedimentation Rate, White Blood Cell and Differential White Cell Counts in Patients Diagnosed with Rheumatoid Arthritis in Owerri, Nigeria, *SAR J Anat Physiol*, *6*(1), 1-7.

1. INTRODUCTION

Rheumatoid arthritis (RA) is a chronic immune-mediated systemic inflammatory disease characterized by chronic synovial inflammation and hyperplasia, which drive joint erosion and damage, and a range of systemic manifestations, which contribute to overall disease burden (McInnes and Schett, 2015). It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen following rest. Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body. The disease may also affect other parts of the body, including skin, eyes, lungs, heart, nerves and blood (Dessie *et al*., 2021). This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart. Fever and low energy may also be present. Often, symptoms come on gradually over weeks to months.

While the cause of rheumatoid arthritis is not clear, it is believed to involve a combination of genetic and environmental factor (Dessie *et al*., 2021). The Underlying mechanism involves the body's immune system attacking the joints. This results in inflammation and thickening of the joint capsule. It also affects the underlying bone and cartilage. The diagnosis is made mostly on the basis of a person's signs and symptoms (McInnes and Schett, 2015). X-rays and laboratory testing may support a diagnosis or exclude other diseases with similar symptoms. Other diseases that may present similarly include systemic lupus erythematosus, psoriatic arthritis, and fibromyalgia among others.

The goals of treatment are to reduce pain, decrease inflammation, and improve a person's overall functioning (Messemaker *et al.,* 2015). This may be helped by balancing rest and exercise, the use of splints and braces, or the use of assistive devices. Pain medications, steroids, and Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used to help with symptoms. Disease-modifying antirheumatic drugs (DMARDs), such as hydroxychloroquine and methotrexate, may be used to try to slow the progression of disease. Biological DMARDs may be used when disease does not respond to other treatments. However, they may have a greater rate of adverse effects. Surgery to repair, replace, or fuse joints may help in certain situations (Schett and Firestein, 2020). The most common haematologic manifestations of RA is mild anaemia with haematocrit values in the range of 30 - 34 percent. This has been recorded in 25 - 35 percent of patients. It is characterized by low concentration of serum -iron and low serum iron binding capacity and does not respond to oral iron. The chronic anaemia may be complicated by true iron deficiency secondary to gastrointestinal blood loss from those treats with analgestic and anti-inflammatory drugs (Denesi and Taccam, 2014). White blood cells may be within the normal range or slightly elevated, but hih counts have been recorded by past researchers. Increase in neutrophils has equally been recorded as well as raised basophil counts (Harrison, 2021). Leucopenia though very rare could be observed in a chronic state. There may be a shift to the left in neutrophilia. Eosinophilia has been reported in most studies.

In general, CRP plays an important role in host defence mechanisms against infectious agents and in the inflammatory response (Murphy ad Hutchinson, 2017). CRP binding to immunoglobulin Fc gamma receptors (FcgR) promotes the production of proinflammatory cytokines leading to an amplification loop of inflammation (Berendsen *et al*., 2017). It is produced predominantly by hepatocytes in response to stimulation by IL-6, but CRP has also been reported to be expressed by smooth muscle cells, macrophages, endothelial cells, lymphocytes, and adipocytes (Philippou and Nikiphorou, 2018). There has been controversy over the direct role of CRP in inflammation and infection, but the identification of CRP isoforms with different biological properties provided a potential explanation for conflicting observations (Yoshii *et al*., 2018).

2. MATERIALS AND METHODS

2.1 Study Area

The study was carried out at Federal University Teaching Hospital, Owerri, Imo State, Nigeria.

2.2 Study Design

This was a cross-sectional study carried out from the month of June to August, 2023, and all subjects who gave their informed consent and completed the questionnaire were enrolled in the study. The study population consisted of 50 rheumatoid arthritis patients and an equivalent number of age - matched non-rheumatoid arthritis patients who served as the controls. Blood samples were collected from eligible subjects and the procedures were carried out at the Federal University Teaching Hospital, Owerri. Standard operating procedures were used, and the manufacturers' instructions were strictly followed. The results of the tests were analyzed using SPSS version 21.

2.3 Sample Collection

Eight milliliters of venous blood sample was collected at the ante-cubital vein aseptically, 4ml was dispensed into ethylenediaminetetraacetic acid containers for the estimations of ESR, TWBC and differential white cell counts, while the remaining 4ml was dispensed into plain containers for C- reactive protein estimation. The EDTA and plain containers were properly labeled with the subject's name, sample number and date of collection. The blood dispensed into the EDTA containers was stored in a refrigerator at 4^0C while the serum was stored in a freezer at -20^0C prior to use.

2.4 Ethical Consideration

The study was approved by the ethics and research committee of Federal University Teaching Hospital, Owerri. All study participants who gave their informed consent were enrolled in the study and samples were taken.

2.5 Laboratory Analysis

The determination of erythrocyte sedimentation rate was done using the Westergren method. The WBC and differential white cell counts were estimated manually, while the C - Reactive protein was estimated using the enzyme - linked immunosorbent assay (ELISA) method.

2.6 Statistical Analysis

The generated data was systematically analyzed as appropriate for means, standard deviation, Pearson correlation and Student's-test on SPSS software version 21 (California Inc.). Results were presented as mean ± standard deviation. A two-sided $p< 0.05$ was considered statistically significant.

3. RESULTS

The mean values of TWBC, (15.04±13.97) cells/µl, neutrophils (62.67±16.08) %, eosinophils (5.47±3.39) %, and monocytes (4.70±3.12)% were significantly raised in rheumatoid arthritis patients when compared to controls (8.93±2.35) cells/µl, (51.52±10.79)%, (28.07±10.12)%, (3.28±2.54)% and (1.80±1.29)% (t=2.91, p=0.031; t=0.08, p=0.000; t=0.01, p=0.001 and t=0.06 p=0.002).

The mean value of lymphocytes (40.48±10.92) % was significantly reduced in rheumatoid arthritis patients when compared to controls (51.52±10.79)% (t=0.85, p=0.000).

Table 1: Mean Values of WBC, Neutrophils, Lymphocytes, Eosinophils and Monocytes in Rheumatoid Arthritis Compared to Controls

Parameter	Test n=50	Control n=50	t-value	p-value
WBC (cells/µl)	15.04±13.97	8.93±2.35	2.19	0.031*
Neutrophils (%)	62.67±16.08	51.52±10.79	0.08	0.000*
Lymphocytes (%)	28.07±10.12	40.48±10.92	0.85	0.001*
Eosinophils (%)	5.47±3.39	3.28±2.54	0.01	0.002*
Monocytes (%)	4.70±3.12	1.80±1.29	0.06	0.000*

Key
WBC: White Blood Cell
***:** Significant

The mean values of ESR (50.16±40.87) mm/hr and C-reactive protein (79.16±55.55) mg/dl were significantly higher in rheumatoid arthritis patients when compared to controls (6.89±2.09) mm/hr and (8.32±3.03) mg/dl respectively (t=0.07, p=0.000 and t=0.08, p=0.001).

Table 2: Mean Values of ESR and C-reactive Protein in Rheumatoid Arthritis Versus Controls

Parameter	Test n=50	Control n=50	t-value	p-value
ESR (mm/hr)	50.16±40.87	6.89±2.09	0.07	0.000*
C-reactive protein (mg/dl)	79.16±55.55	8.32±3.03	0.08	0.001*

Key
ESR: Erythrocyte Sedimentation Rate
***:** Significant p-value

There were no significant differences in the mean values of WBC (15.04+10.88) cells/µ1, neutrophils (63.86+15.09)%, lymphocytes(41.89+ 11.08)%, eosinophils (5.11+4.09)%, monocytes(4.86+2.86)%, ESR (55.19+37.76%)mm/hr and C-reactive protein (80.56+4055)mg/dl in male rheumatoid arthritis patients compared to females (14.88+13.98)cells/µl, (62.77+13.22)%,(40.77±8.76) %,(4.99±4.83) %, (4.67+4.01)%, (58.76+36.87)mm/hr and (81.56+21.09)mg/dl, respectively (t=1.78, p=0.886; t=1.77, p=0.695; t=1.69, p=0.881; t=0.07, p=0.652; t=1.44, p=0.341; t=6.79, p=0.516 and t=7.17, p=0.434).

Table 3: Comparison of the Mean Values of WBC, Neutrophils, Lymphocytes, Eosinophils, Monocytes, ESR and C-reactive Protein in Male Versus Female Rheumatoid Arthritis patients

Parameter	Male n=25	Female n=25	t-value	p-value
WBC (cells/µl)	15.04±10.88	14.89±13.98	1.78	0.886
Neutrophils (%)	63.86±15.09	62.77±13.22	1.77	0.695
Lymphocytes (%)	41.89±11.08	40.77±8.76	1.69	0.881

Parameter	Male n=25	Female n=25	t-value	p-value
Eosinophils (%)	5.11±4.09	4.99±4.83	0.07	0.652
Monocytes (%)	4.86±2.86	4.67±4.01	1.44	0.341
ESR (mm/hr)	55.19±37.76	58.76±36.87	6.79	0.516
C-reactive protein (mg/dl)	80.56±40.55	81.56±21.09	7.17	0.434

Key
ESR: Erythrocyte Sedimentation Rate
WBC: White Blood Cell

There was a significant positive correlation of C-reactive protein with ESR, WBC, and neutrophils in rheumatoid arthritis patients (r=0.32, p=0.011, r=0.44 and p=0.021, r=0.54, p=0.043), and a non-significant positive correlation with lymphocytes, monocytes and eosinophils (r=0.87, p=0.179, r=0.96, p=0.317 and r=1.06, p=0.398).

Table 4: Correlation of C-reactive Protein with ESR, WBC, Neutrophils, Lymphocytes, Monocytes and Eosinophils in Rheumatoid Arthritis Patients

Variable	N	r	p-value
ESR	50	0.32	0.011*
WBC	50	0.44	0.021*
Neutrophils	50	0.54	0.043*
Lymphocytes	50	0.87	0.179
Monocytes	50	0.96	0.317
Eosinophils	50	1.06	0.398

Key
ESR: Erythrocyte Sedimentation Rate
WBC: White Blood Cell
***:** Significant

4. DISCUSSION

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease diagnosed mostly by presenting articular manifestations. Patients with rheumatoid arthritis (RA) have a two-fold increased risk of morbidity and mortality for cardiovascular (CV) disease (Taleb, 2016).

In the present study the mean values of WBC, neutrophils, eosinophils and monocytes were significantly higher in rheumatoid arthritis patients when compared to controls. The significant increas might be due to the active role they play in the inflammatory process of rheumatoid arthritis. According to the report by Ertenli *et al*., (2013), the levels of TWBC, neutrophils, eosinophils and monocytes are positively correlated with high disease activity of rheumatoid arthritis. The result of this study is also in agreement with the report by Viatte *et al*., (2013), who reported an increase in the mean values of eosoniphils and monocytes in patients with active rheumatoid arthritis.

The mean value of lymphocytes was significantly reduced in rheumatoid arthritis patients when compared to controls. Several authors have reported that lymphopenia is commonly seen in patients with rheumatoid arthritis patients and this might be due to a depression in circulating T-cell numbers due to inflammation, for example, the study carried out by Symmons *et al*., (2019), reported a similar finding.

The current study reveals that the mean value of ESR was significantly raised in rheumatoid arthritis patients when compared to controls. ESR is widely used as an indicator of acute-phase response in several immune-mediated inflammatory diseases, including rheumatoid arthritis. The increase in ESR level in patients with rheumatoid arthritis reflects an inflammatory activation or an acute-phase response, accompanied by raised levels of circulating pro-inflammatory cytokines and their receptors, which in turns causes an increase in ESR. This observation is consistent with the findings carried out by Maradit-Kremers *et al*., (2017), who stated that "disease activity in rheumatoid arthritis is assessed by examining symptoms of inflammatory joint disease, functional status and various laboratory tests of immune activation, such as erythrocyte sedimentation rate (ESR). Though they noted that the ESR is not diagnostic of any particular disease, it is an inexpensive and a practical indicator of response of acute phase proteins in plasma Beighton *et al*., (2015).

The present study reveals that the mean value of the C-reactive protein was significantly higher in rheumatoid arthritis patients when compared to controls. C-reactive protein (CRP) is mainly classed as an acute marker of inflammation, but research is starting to indicate important roles that CRP plays in inflammation. CRP is the principal downstream mediator of the acute-phase response following an inflammatory event and is primarily synthesized by IL-6-dependent hepatic

biosynthesis (Baumeister *et al*., 2016). The main role of CRP in inflammation tends to focus around the activation of the C1q molecule in the complement pathway leading to the opsonization of pathogens. Although CRP can initiate the fluid phase pathways of the host defense by activating the complement pathway, it can also initiate cell-mediated pathways by activating complement as well as to binding to Fc receptors of IgG (Braig *et al*., 2017). CRP binds to Fc receptors with the resulting interaction leading to the release of pro-inflammatory cytokines. CRP also has the ability to recognize self and foreign molecules based on the pattern recognition, something that other activators of complement such as IgG cannot achieve because these molecules only recognize distinct antigenic epitopes (Braig *et al*., 2017). The result of this study is in agreement with the report by Sproston *et al*., (2018), who stated that rheumatoid arthritis is associated with increases in C-reactive protein.

There was no significant difference in the mean values of WBC, neutrophils, lymphocytes, eosinophils, monocytes, ESR and C-reactive protein in male rheumatoid arthritis patients when compared to the females. The result indicates that sex is not predisposing factor in rheumatoid arthritis disease. Though a study carried out by Favalli *et al*., (2019) revealed that females are more likely to be affected by rheumatoid arthritis (RA) than males. He further stated that hormonal and genetic factors may contribute to sexual variation in the prevalence of RA.

Lastly, from this study, there was a significant positive correlation of C-reactive protein with WBC, ESR, neutrophils, lymphocytes, monocytes and eosinophils in rheumatoid arthritis patients. This is in consonance with the study reported by Balestrino *et al.*, (2018), who stated that white blood cell count, CRP and erythrocyte sedimentation rate correlate with outcome in patients with inflammatory disease condition.

5. CONCLUSION

Based on this research it can be concluded that rheumatoid arthritis is associated with increase in total white blood cell, neutrophils, eosinophils, monocytes, ESR and C-reactive protein. Lymphocytopenia is linked to rheumatoid arthritis, and significant relationships exist among C-reactive protein, ESR, WBC and neutrophils in rheumatoid arthritis.

REFERENCES

- Aho, K., Heliovaara, M., Maatela, J., & Tuomi, T. (2016). Rheumatoid factors antedating clinical rheumatoid arthritis. *Journal of Rheumatoid*, *18*, 1282-1284.
- Ajayi, H. (2016). Antioxidant Enzymes and Acute Phase Proteins Correlate with Marker of Lipid Peroxide in Adult Nigerian ulcer Patients, *Iranian Journal of Basic Medical Sciences Autumn*, *13*(4), 177-182.
- Aletaha, D., Neogi, T., Silman, A. J., & Funovits, J. (2015). Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League against Rheumatism collaborative initiative. *Arthritis Rheumatoid*, *62*, 2569–2581.
- Al-Marri, M. R., & Kirkpatrick, M. B. (2015). Erythrocyte sedimentation rate in childhood tuberculosis: is it still worthwhile? *International Journal of Tubercle Lung Diseases*, *4*(3), 237-239.
- Amezcua-Guerra, L. M., Castillo-Martinez, D., & Bojalil, R. (2015). The story behind the acute-phase reactants. *Journal of Rheumatology*, *37*(2), 469.
- Araoye, M. O. (2004). Research methodology with statistics for health and social sciences. Ilorin, Nigeria: *Nathadex publishers*, *11*, 98 – 100
- Balestrino, M., Partinico, D., Finocchi, C., & Gandolfo, C. White blood cell count and erythrocyte sedimentation rate correlate with outcome in patients with acute ischemic stroke. *Journal of* Stroke *Cerebrovasc Diseases*, *7*(2), 139-44.
- Baumeister, D., Akhtar, R., Ciufolini, S., Pariante, C. M., & Mondelli, V. (2016). Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, inetleukin-6 and tumour necrosis factor-α. *Mol Psychiatry*, *21*, 642–649.
- Beighton, P., Solomon, L., & Valkenburg, H. (2015). Rheumatoid arthritis in a rural South African Negro population. *Annals of Rheumatologic Discussions*, *34*(2), 136-141.
- Berendsen, M. L., van Maaren, M. C., Arts, E. E., & den Broeder, A. A. (2017). Anticyclic citrullinated peptide antibodies and rheumatoid factor as risk factors for 10-year cardiovascular morbidity in patients with rheumatoid arthritis: a large inception cohort study. *Journal of Rheumatology*, *44*(9), 1325–1330.
- Bonora, E., Kiechl, S., & Willeit, J. (2013). Metabolic syndrome: epidemiology and more extensive phenotypic description. Cross-sectional data from the Bruneck study. *International Journal of Obesterics Related Metabolic Disorder*, *27*, 1283–1289.
- Braig, D., Nero, T. L., Koch, H. G., & Kaiser, B. (2017). Transitional changes in the CRP structure led to the exposure of proinflammatory binding sites. *National Community*, *8*, 14188- 101038
- Cheesbrough, M. (2007). District Laboratory Practice in Tropical Countries. Cambridge, UK: *Cambridge University Press*, *24*, 314 - 318.
- Chessbrough, M. (2007) District Laboratory practice in tropical countries ECedition. *Cambridge University Pressm*, *2*, 80 -85.
- Cylwik, B., Chrostek, L., Gindzienska-Sieskiewicz, E., & Sierakowski, S. (2020). Relationship between serum acute-phase proteins and high disease activity in patients with rheumatoid arthritis. *Advanced Medical Science*, *55*, 80–85

- De Silva, D. A., Woon, F. P., & Chen, C. (2014). Serum erythrocyte sedimentation rate is higher among ethnic South Asian compared to ethnic Chinese ischemic stroke patients. Is this attributable to metabolic syndrome or central obesity? *Journal of Neurological Science*, *276*, 126–129.
- Denesi, T. H. (2014). Haematology toxicity of Immunosuppressive Treatment. *Transplant, 36*, 703- 4.
- Dessie, G., Tadesse, Y., Demelash, B., Genet, S., & Malik, T. (2021). Evaluation of C-Reactive Protein and Associated Factors Among Patients Suffering from Rheumatoid Arthritis at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. *Open Access Rheumatology*, *13*, 247-255.
- Dorner, K., Egerer, E., Feist, G. R., & Burmester, Q. (2014). Rheumatoid factor revisited. *Current Opinion on Rheumatology*, *16*, 246–253.
- Dougados, M. (2014). Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Annals of Rheumatoid Diseases*, *73*, 62–8.
- Emery, P., Breedveld, F. C., Dougados, M., Kalden, J. R., & Schiff, M. H. (2016). Early referral recommendation for newly diagnosed rheumatoid arthritis: evidence-based development of a clinical guide. *Annual Rheumatoid Disease*, *61*, 290-297.
- Ertenli, I., Kiraz, S., Oztürk, M. A., & Haznedarolu, I. (2013). Pathologic leucocytosis of rheumatoid arthritis. *Rheumatology*, *23*(2), 49–60.
- Ertenli, I., Kiraz, S., Oztürk, M. A., & Haznedarolu, I. (2013). Pathologic leucocytosis of rheumatoid arthritis. *Rheumatology*, *23*(2), 49–60.
- Fabry, T. L. (2017). Mechanism of erythrocyte aggregation and sedimentation. *Blood*, *70*, 1572–1576.
- Favalli, E. G., Biggioggero, M., Crotti, C., Becciolini, A., & Raimondo, M. G. (2019). Meroni PL. Sex and management of rheumatoid arthritis. *Clinical Reviews of Allergy Immunology*, *56(*3), 333–345.
- Firestein, G. S. (2015). Evolving concepts of rheumatoid arthritis. *Nature*, *423*(6937), 356-361.
- Geffken, D. F., Cushman, M., & Burke, G. L. (2016). Association between physical activity and markers of inflammation in a healthy elderly population. *America Journal of Epidemiology*, *153*, 242–250.
- Harrison, E. D. (2021). Chemical features of rheumatoid arthritis, Textbook of Rheumatology£fh edition W. B. *Saunders Philadelphia*, *2*, 167-169.
- Hill, J. A., Southwood, S. A., Sette, A. M., Jevnikar, D. A., & Bell, E. (2013). Cairns, Cutting edge: the conversion of arginine to citrulline allows for a high-affinity peptide interaction with the rheumatoid arthritis-associated HLA-DRB1*0401 MHC class II molecule. *Journal of Immunology*, *171*(23), 538–541.
- Ishida, K., Kimura, F., Imamaki, M., Ishida, A., Shimura, H., Kohno, H., & Sakurai, M. (2016). Relation of inflammatory cytokines. *European Journal of Cardio-thoracic Surgery*, *29(*4), 501–505.
- Jou, J. M., Lewis, S. M., & Briggs, C. (2016). ICSH review of the measurement of the erythocyte sedimentation rate. *International Journal of Laboratory Hematology*, *33*, 125–132.
- Kraan, M. C., Versendaal, H., & Jonker, M. (2018). Asymptomatic synovitis precedes clinically manifest arthritis. *Arthritis Rheumatoid*, *41*, 1481-1488
- Lawrence, J. S. (2013). Sources of error in the erythrocyte sedimentation rate. *Annals of Rheumatoid Disease*, *12*(3), 206-211.
- Lindqvist, E., Eberhardt, K., Bendtzen, K., Heinegard, D., & Saxne, T. (2015). Prognostic laboratory markers of joint damage in rheumatoid arthritis. *Annals of Rheumatoid*, *64*(2), 196-201.
- Maradit-Kremers, H., Nicola, P., Crowson, C., & Roger, S. (2017). Raised erythrocyte sedimentation rate signals heart failure in patients with rheumatoid arthritis. *Annals of Rheumatoid Disorder*, *66*, 76–80.
- Masi, A. T., Aldag, J. C., & Sipes J. (2017). Do elevated levels of serum C-reactive protein predict rheumatoid arthritis in men: correlations with pre-RA status and baseline positive rheumatoid factors. *Journal of Rheumatology*, *28*, 2359-2361.
- McInnes, I. B., & Schett, G. (2015). The pathogenesis of rheumatoid arthritis. *National England Journal of Medicine*, *365*, 2205–2219.
- Messemaker, T.W., Huizinga, F., & Kurreeman, A. (2015). Immunogenetics of rheumatoid arthritis: understanding functional implications, *Journal of Autoimmune*, *64*(5), 74–81.
- Murphy, D. (2017). Hutchinson D. Is male rheumatoid arthritis an occupational disease? A review. *Open Rheumatology Journal*, *11*, 88.
- Naranj, A., Toloza, S., Guimaraes, W., da Silveira, I. (2015). Smokers and non smokers with rheumatoid arthritis have similar clinical status: data from the multinational QUEST-RA database. *Clinical Experimental Rheumatology*, *28*, 820–27.
- Nigeria population commission (NPC), (2006). Census. Retrieved from the vanguard newpaper.
- Ohmura, K. C., Terao, E., Maruya, M., Katayama, K., & Matoba, K. (2020). Anticitrullinated peptide antibody-negative RA is a genetically distinct subset: a def initive study using only bone-erosive ACPA-negative rheumatoid arthritis. *Rheumatology*, *49*(12), 2298–2304
- Orr, C. K., Najm, A., Young, F., McGarry, T., Biniecka, M., Fearon, U., & Veale, D. J. (2018). The Utility and Limitations of CRP, ESR and DAS28-CRP in Appraising Disease Activity in Rheumatoid Arthritis. *Front Medicin*e, ***5***, 185
- Philippou, E., & Nikiphorou, E. (2018). Are we really what we eat? Nutrition and its role in the onset

of rheumatoid arthritis. *Autoimmune Revision*, *17*(11), 1074–1077.

- Pinto, A., Di Raimondo, D., & Tuttolomondo, A. (2017). Effects of physical exercise on inflammatory markers of atherosclerosis. *Current Pharmaceuticals*, *18*, 4326–4349.
- Pope, J. E., & Choy, E. H. (2021). Seminars in Arthritis and Rheumatism. *Rheumatoid Journal*, *51*, 219-229.
- Reed, E., Jiang, X., Kharlamova, N. and Ytterberg, A.I. (2016). Antibodies to carbamylated alpha-enolase epitopes in rheumatoid arthritis also bind citrullinated epitopes and are largely indistinct from anti-citrullinated protein antibodies. *Arthritis Research*, *18*(8), 96.
- Romero, A., Muñoz, M., & Ramírez, G. (2013). Length of sedimentation reaction in blood: a comparison of the test 1 ESR system with the ICSH reference method and the sedisystem 15. *Clinical Chemistry Laboratory Medicine, 41*, 232–237.
- Roseman, C., Truedsson, L., & Kapetanovic, M. C. (2017). The effect of smoking and alcohol consumption on markers of systemic inflammation, immunoglobulin levels and immune response following pneumococcal vaccination in patients with arthritis. *Arthritis Research*, *14*, 170.
- Scally, S.W., Petersen, J. S., Law, N. L., Dudek, H. J., 7 Nel, K. L. (2013). A molecular basis for the association of the HLA-DRB1 locus, citrullination, and rheumatoid arthritis, *Journal of Experimental Medicine*, *210*(13), 2569–2582.
- Schett, G. S., & Firestein, M. (2020). Classic and alternative views on the pathogenesis of rheumatoid arthritis. *Annals of Rheumatoid Disease*, *69*(2), 787–789.
- Smolen, J. S., Aletaha, D. S., & McInnes, I. B. (2016). Rheumatoid arthritis. *The Lancet*, *388*(10055): 2023-2038.
- Sproston, N. R., & Ashworth, J. J. (2018). Role of C-Reactive Protein at Sites of Inflammation and Infection. *Frontier Immunology*, 139, 754.
- Stock, W., & Hoffman, R. (2016). White blood cells I: non-malignant disorders. *Lancent*, *355*, 1351-1357.
- Sykes, W.O. (2013). Erythrocyte sedimentation rate: the effect of alcohol as contaminant. *British Medical Journal*, *1*, 393–394.
- Symmons, D. M., Farr, M. D., & Salmon, P. A. (2019). Anaemia and Lymphopenia in rheumatoid arthritis. *Journal of the Royal Society of Medicine*, *3*, 462-463.
- Taleb, T. (2016). Work disability in early rheumatoid arthritis. *Clinical Express and Rheumatoid*, *21*(5), 71-74.
- Van Steenbergen, W., Mangnus, L., Reijnierse, M., & Huizinga, A. H. (2016). Clinical factors, anticitrullinated peptide antibodies and MRI-detected subclinical inflammation in relation to progression from clinically suspect arthralgia to arthritis. *Annals of Rheumatoid Disease, 75*(16), 1824–1830.
- Viatte, S., Plant, D., & Raychaudhuri, S. (2013). Genetics and epigenetics of rheumatoid arthritis. *National Review of Rheumatology*, *9*(3), 141-153.
- Yoshii, I., Chijiwa, T., &Sawada, N. (2018). Influence of pain score measured by a visual analog scale (PS-VAS) on the Health Assessment Questionnaire Disability Index and 28-joint Disease Activity Index with C-reactive protein in rheumatoid arthritis patients. *International Journal of Rheumatoid Disease*, *21*(11), 1955–1961.