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Evaluation of Serum Antinuclear Antibodies and Uric Acid in Some Rheumatoid Arthritis Patients in Kano Metropolis

***Isah SY[1], Ifeanyi V[1], Gwaram BA[2], Hamid KM[3], Saidu H[1], Okafor PA[4], Kabir N[5], Nnodim JK[6]**

[1]Department of Medical Laboratory Science,
Faculty of Allied Health Sciences,
Bayero University,
P.M.B. 3011, Kano, Nigeria

[2] Department of Medicine,
Faculty of Clinical Sciences,
Bayero University.
P.M.B. 3011, Kano, Nigeria

[3]Department of Immunology,
School of Medical Laboratory Sciences,
Usmanu Danfodiyo University,
P.M.B.2346, Sokoto, Nigeria

[4]School of Medical Laboratory Science,
Ahmadu Bello University Teaching Hospital,
P.M.B.06, Shika, Kaduna, Nigeria

[5]Department of Biochemistry,
Federal University Dutse,
P.M.B 7156, Jigawa State, Nigeria.

[6]Department of Medical Laboratory Science,
Faculty of Health Sciences,
Imo State University,
PMB 2000 Owerri, Imo State, Nigeria

Email: isyahaya.mls@buk.edu.ng

Abstract

Rheumatoid arthritis (RA) is an inflammatory progressive disease associated with severe pain, joint destruction and disability if diagnosed late and not treated appropriately. The aim of the study was to evaluate serum Anti-nuclear antibodies (ANA) and Uric acid (UA) level in patients with rheumatoid arthritis in Kano Metropolis. A total of 134 RA patient and 56 apparently healthy controls were used for the study, males were 54 while females were 80 aged between 25-85 years. Blood samples was

**Author for Correspondence*

collected from the participants, serum UA and ANA were analysed using enzymatic colorimetric method, Randox manual reagent kit (UK) and Enzyme linked immunosorbent assay technique Product of perfemed-ANA Elisa kits, (USA) respectively, SPSS software package version 21 was used for the analysis of data. Our findings showed that, the higher percentage frequency of 17(25.9 %) were observed in patients of ages 45-54 while lower frequencies of 2(3.0%) were observed in patients between the ages 25-34 years. The mean values of serum UA and ANA were significantly higher ($p<0.05$) in patient group than the control while female with RA had significantly increased ($p<0.05$) ANA compared with the male patients. However, male had increased uric acid compared with the female, with no statistical significant. There was significant relationship ($p<0.05$) between serum uric acid and ANA in RA patients. Our results revealed that, females had higher prevalence of RA than males with increased serum UA and ANA. Hence, patients presented with symptoms of RA might be recommended for UA and ANA among other investigations, this may help in the management of RA patients.

Keywords: Anti-nuclear antibodies, Kano, Metropolis, Rheumatoid arthritis, Uric acid.

INTRODUCTION

The complexity of rheumatoid arthritis (RA) itself makes its diagnosis, prognosis and management difficult; hence an early diagnosis of RA becomes critical to avoid further complications and disabilities in developed and developing countries (Madav *et al*., 2020). Immune system abnormalities are the main cause of this disease, which is associated with inflammation of the synovial membranes that causes painful inflammation of the joints (Manole *et al*., 2010). Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes inflammation of the joints characterized by swelling and pain (Fleischmann *et al*., 2012*)*. It is characterized by a symmetrical polyarticular inflammation of the synovial membrane, typically of the small joints of the hands, wrist and feet (David *et al*., 2010). This inflammation leads to progressive joint damage which leads to deformities and loss of function. In addition, chronic inflammation secondary to rheumatoid arthritis can also lead to higher risk of cardiovascular disease and abnormalities in bone metabolism (Michelle *et al*., 2011). Rheumatoid arthritis is regarded as the most common inflammatory arthritis with prevalence of 0.5%-1% (Guo *et al*., 2018) in industrialized nations and an estimate of 0.2-0.3% in Africa (Adelowo *et al*., 2010; Dowman *et al*., 2012). Clinical signs and symptoms of rheumatoid arthritis may accumulate to include pain or pain in more than one joint, stiffness in more than one joint, tenderness and swelling in more than one joint, the same symptoms in both sides of the body (such as both hands or on both knees), weight loss, fever, tiredness or fatigue, weakness (Shiel and Driver, 2015). Symptoms severity and rigorousness of RA can differ from person to person, some may experience mild–moderate forms with periods of flares and remission, while others may have severe forms, which stay active most of the time and last a lifetime (Cojocaru*et al.,* 2010). Nevertheless, the cause of RA remains uncertain, but may be attributed to the combination of genetic and environmental factors, such as female gender, family history thought to be linked with the etiology of RA (Gibosfky, 2014).

Antinuclear antibodies (ANA) are autoantibodies that react with nucleoplasm antigens (Smeenk *et al*., 2002). Autoantibodies such as antidouble stranded DNA (anti-dsDNA) and anti-Smith antigen (anti-Sm) among others are a common feature in rheumatic autoimmune diseases (Steiner and Smolen, 2002). Antinuclear antibody can also be caused by chronic infections, especially virus, also toxic agents and drugs among others (Gangarathna and Khalid, 2017).

Uric acid (UA) is an end product of exogenous pool of purines and endogenous purine metabolism in humans (Stanich *et al*., 2009). It was thought to have a beneficial role by acting as an antioxidant (Panoulas *et al*., 2008). The exogenous pool varies significantly with diet, and animal proteins contribute significantly to this purine pool while endogenous production is mainly from the liver, intestines etc (El-ridi and Tallima, 2017). An excess of this bodily waste product in our circulation may cause gout by building up and forming monosodium urate crystals which is deposited in joints, causing pain, inflammation, make blood and urine becoming too acidic among others (Martillo *et al*., 2014). The aim of this study was to evaluate serum anti-nuclear antibodies and uric acid levels in patients with rheumatoid arthritis in some hospitals in Kano Metropolis.

MATERIALS AND METHODS

This study was conducted in Kano State. Kano state lies between latitude $10^0$33'N and $12^0$33E and longitudes $7^0$45'N and $9^0$29'E and also lies at about 1580 feet above sea level, it is bordered by Katsina to the north-west, Jigawa state to the north-east and Kaduna state to the southern (Ibrahim and Muhammed, 2016). The study was a case control study evaluating serum uric acid and serum antinuclear antibodies in rheumatoid arthritis patients in Aminu Kano teaching hospital and Abdullahi wase specialist hospital in Kano metropolis. The study comprised of one hundred and thirty four (134) RA patients and fifty six (56) apparently healthy volunteers who were used as controls. Both clinical and laboratory investigation confirmed those patients with rheumatoid arthritis. The Serum UA was measured by enzymatic colorimetric method Randox Manual as described by Fossati *et al*. (1980). The Serum ANA was measured using the technique described by ELISA Product of perfemed-ANA Elisa kits (USA).

Statistical Analysis

Data was analyzed using SPSS version 21.0 statistical software. The Mean and Standard Deviation were computed and results were expressed as mean±SD. Student un-paired t-test was used to compare differences between means. The Chi-square test was used for testing the significance of relationships between categorical variables. Statistical significance was set at $p<0.05$.

Ethical Consideration

This study was approved by the ethical committee of Aminu Kano Teaching Hospital Kano and Ministry of health Kano state with reference number AKTH/MAC/SUB/12A/P-3/VI/2666 and MOH/Off/797/T.I/1447 respectively. The research was conducted in Aminu Kano teaching hospital and Nasarawa specialist hospital. The purpose and the procedure of the study were explained to all participants and a written informed consent was obtained from the participants before samples were collected.

RESULTS

The results obtained from the present study are presented in tables 1-6 respectively. Table 1 depict the distribution of patients with Rheumatoid Arthritis (RA) based on Age. The participants age ranges were between 25-84 years, the higher frequency was observed in age group 45- 54 years with percentage frequency (25.9%), while the lower frequency was observed in age group 25-34 with percentage frequency (3.0%).

The Serum antinuclear antibodies (ANA) in patients with RA compared with control subjects. The mean values of ANA was statistically higher ($p=0.026$) in the patient group

with (1.12±0.97) when compared with the control group with (0.54±0.20). The higher frequency of ANA was observed in <0.9 with percentage frequency 88 (65.7%), while the lower frequency was observed in 0.9-1.1 with percentage frequency 16 (11.9%) as shown in table 2.

Table 3 shows the comparison of serum antinuclear antibodies (ANA) in male and female patients with RA. The mean values of ANA was higher in female (1.18±1.01) group, compared with the male (0.87±0.77) group but no statistical significant (p=0.246). However, the higher frequency of patients was observed in female (50) and the lowest frequency was observed in male (6).

Serum UA in patients with RA compared with control subjects, the mean value of UA was statistically significantly higher (p=0.00) in the patient group with (524.1±135.4) when compared with the control group with (385.2±147.3). However, the higher frequency of 40 (29.9%) was observed patients in the range of 400µmol/l -499 µmol/l and 500 µmol/l -599 µmol/l respectively and the lowest frequency of 0(0%) was observed controls in the range of between 600 µmol/l -699 µmol/l and 700 µmol/l and above respectively as depited in table 4.

Table 5 showed the comparison of serum uric acid (UA) in male and female patients with RA. The mean values of UA was higher in male group (550±113.4), when compared with the female group (508±149.2) with no statistical significant (p=0.691). However, the higher frequency of 22 was observed in females with UA within the range of 400 µmol/l-499 µmol/l and the lowest frequency of 0 was observed in males with UA within the range of 200 µmol/l -299 µmol/l.

Table 6 shows the relationship between Serum UA and Serum antinuclear antibodies in RA patients. There was statistical relationship between Serum UA and ANA in different index range in RA patients (X^2 =19.892, p=0.030).

Table 1: Distribution of patients with rheumatoid arthritis based on age

Age (years)	Frequency (%)
25-34	4 (3.0)
35-44	32(23.4)
45-54	34(25.9)
55-64	26(19.4)
65-74	30(22.4)
75-84	8(6.0)

F= Frequency, %= Percentage

Table 2: Serum antinuclear antibodies (ANA) in patients with Rheumatoid Arthritis compared with control subjects.

ANA index	Patient (n=134) Frequency (%)	Control (n=56) Frequency (%)	*t- test*	*p*-value
<0.9	88 (65.7)	56(100.0)		
0.9-1.1	16 (11.9)	0(0)	2.353	0.026*
>1.1	30(22.4)	0(0)		
Mean±SD	1.12 ± 0.97	0.54 ± 0.20		

p≤ 0.05 (significant of t-test) for patient vs. control analysis;, %= Percentage, (<0.9=negative for ANA, 0.9-1.1= weakly positive, >1.1 strongly positive for ANA.)*

Table 3: Comparison of serum antinuclear antibodies (ANA) in male and female patients with Rheumatoid Arthritis

ANA index	Male	Female	*t-test*	*p*-value
<0.9	38	50		
0.9-1.1	6	10	1.185	0.246
>1.1	10	20		
M±SD	0.87±0.77	1.18±1.01		

p≤ 0.05 (significant of t-test)(<0.9=negative for ANA, 0.9-1.1= weakly positive, >1.1 strongly positive for ANA)

Table 4: Serum Uric acid (UA) in patients with Rheumatoid Arthritis compared with control subjects

Serum UA µmol/l	Patient (n=134) Frequency (%)	Control (n=56) Frequency (%)	*t-test*	*p*-value
200-299	4(3.0)	8(14.3)		
300-399	18(13.4)	22(39.3)		
400—499	40(29.9)	24(42.9)	10.556	0.000*
500-599	40(29.9)	2(3.6)		
600-699	10(7.5)	0(0)		
700 & above	22(16.4)	0(0)		
Mean±SD	524.1 ± 135.4	385.2 ± 147.3		

p≤ 0.05 (significant of t-test) for patient vs. control analysis;%= Percentage*

Table 5: Comparison of serum uric acid in male and female patients with Rheumatoid Arthritis

Serum Uric acid (µmol/l)	Male	Female	*t-test*	*p*-value
200-299	0	4		
300-399	2	16		
400-499	18	22	0.402	0.691
500-599	20	20		
600-699	6	4		
700 & above	8	14		
M±SD	550±113.4	508±149.2		

p≤ 0.05 (significant of t-test) for patient vs. control analysis

Table 6: Relationship between Serum Uric Acid and Serum antinuclear antibodies (ANA) in Rheumatoid Arthritis patients.

Serum Uric acid (µmol/l)	ANA index			X^2	*Df*	*p*-value
	<0.9	**0.9-1.1**	**>1.1**			
200-299	2	2	0			
300-399	12	2	4			
400—499	30	4	6	19.892[a]	10	0.030*
500-599	34	2	4			
600-699	6	2	2			
700 & above	4	4	14			

p≤ 0.05 (significant of t-test) for patient vs. control analysis; X^2= Chi square value, df= degree of freedom. (<0.9=negative for ANA, 0.9-1.1= weakly positive, >1.1 strongly positive for ANA.*

DISCUSSION

In the current study, the higher prevalence of rheumatoid arthritis was observed in age range of 45-54years with percentage frequency 25.9%, this is similar to report of Tiraje *et al*. (2018) in Turkey. This may be as a result of selection of T- cells with increased affinity to self-antigens which occurs more often in the age range, these T-cells have been shown to have greater ability to pro-inflammatory, thereby amplifying autoimmunity (Goronzy *et al*., 2012). Another suggestion may be due to higher percentage of younger $CD4^+$ $CD69^+$ subpopulation in the age range and older patients, indicating lower early activation status in older Rheumatoid Arthritis patients (Pawłowska *et al*., 2011).

Our study shows that, the mean values of Antinuclear antibodies was statistically significantly higher in the patient group than the control group. This is in agreement with the finding of Meyer *et al*. (2004) who reported high level of serum anti-nuclear antibodies in rheumatoid arthritis patients as compared to healthy control. It is also in accordance with the results from study conducted by Nishimura *et al*. (2000). These antibodies may occur as a result of immune abnormalities to the persistence of abnormal B- lymphocytes clones that have escaped the repression exerted by normal tolerogenic mechanisms (Jean *et al*., 2001). The elevation of ANA might indicate the possibility of autoimmune disease (Quan-Zhen *et al*., 2011).

Current study reveals that, the mean values of ANA was higher in female groups when compared with the male groups with no statistical significance, thus higher frequency of patients was observed in female and the lowest frequency was observed in male. This is in conformity with the reports of Quan-Zhen *et al*. (2011); Meier *et al*. (2020). Autoimmune diseases are a heterogeneous group of disorders with multifactorial causes (Cho and Feldman, 2015). The common denominator is an immunological reaction which leads to the breakdown, systemic or organ-specific tolerance for the subject's own tissues (Bolon, 2010). Women are less susceptible to infectious diseases than men (Orstavik, 2017), resulting in an increased response to infection, vaccination and trauma with increased production of antibodies and a predominant T helper (Th)2 immune response, while the Th1 response and inflammation are generally more severe in men (Fairweather *et al*., 2008). As a result, women are more prone to autoimmune diseases, often with a higher concentration of anti-nuclear antibodies (Grygiel-Górniakv *et al*., 2018). Moreover, this higher prevalence can also be attributed in part to the X chromosome, which has many genes linked to the immune system. It is beneficial for women to have two X chromosomes, but the price is an increased tendency to develop autoimmunity (Ngo *et al*., 2014).

In this finding, the mean value of uric acid was statistically higher in the patient group compared with the control group. The result is in conformity with study of Vaidya *et al*. (2018) where they found an increased serum uric acid level in rheumatoid arthritis patients as compared with healthy individuals. However, Zhao *et al*., (2018), reported contrary. Uric acid which is the end product of purine catabolism is present in foods and drinks and taking certain medications can also increase the amount of uric acid in the body (Ben Salem *et al*., 2017). An excess of this bodily waste product in the blood can trigger gout and rheumatoid arthritis (Rock *et al*., 2013). It does this by building up and forming urate crystals of monosodium urate (MSU) which pass freely through the double barrier of the synovial membrane into synovial fluid (Martillo *et al*., 2014; Vaidya *et al*., 2018), it may then accumulate in joints, especially in the hands, feet, and elbows and cause pains, inflammation and rheumatoid arthritis (Vaidya *et al*., 2018).

The current findings shows that, the mean values of uric acid in rheumatoid arthritis patients was higher in males when compared with the females with no statistical significance. These findings agreed with the report of Mateos and Gracia. (2000), which

showed women had significantly lower serum uric acid concentration as compared to men. This result may be due to higher renal clearance of urate in women, possibly due to their high plasma estrogen level (Cheung and Lafayette, 2013).Uric acid is dependent on age particularly with increase in body mass and gender (Zhao *et al*., 2018).

Our results suggested that, there is statistically significant relationship between serum uric acids and serum antinuclear antibodies in rheumatoid arthritis patients. Our finding is in consistent with the previous report of Zhao *et al*., (2018), Rheumatoid arthritis occurs when the immune system reacts abnormally by attacking the joints and sometimes the organs, instead of foreign invaders, such as viruses, bacteria among others that enter our body (Nicholson, 2016). Autoantibodies are a general and typical feature of autoimmune rheumatic diseases (Steiner and smolen, 2002). Antinuclear antibodies (ANA) are antibodies (auto) which react with antigens on nuclear, nuclear or perinuclear antigens (Mahler *et al*., 2014). Uric acid is a waste product of purine metabolism which triggers gout (Rock *et al*., 2012). This indicates that, Increase in purine breaks down due to uric acid, result in the reaction of ANA against the increase uric acid subsequently leading to increase autoantibody.

CONCLUSION

Based on the results of this study, it was discovered that, rheumatoid arthritis is more common in older people than in young adults, it is also associated with elevated serum uric acid level and antinuclear antibodies. There is also a relationship between serum uric acid and antinuclear antibodies in rheumatoid arthritis patients. Uric acid and antinuclear antibodies are important diagnostic assay for rheumatoid arthritis patient.

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